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OF
ORGANIC CHEMISTRY

WORKS OF PROF. A. F. HOLLEMAN,

PH.D., LL.D., D.Sc., F.R.S.E.

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BY

A. F. HOLLEMAN, Ph.D., LL.D., D.Sc., F.R.S.E.

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AUTHOR'S PREFACE TO THE SEVENTH ENGLISH EDITION

So long as there is a public to buy it a novel can be reprinted unchanged; but even with an interval of only a few years between successive issues, each new edition of a text-book of chemistry needs not only careful revision, but also the rewriting of some of its chapters.

This fact has rendered it impossible to avoid making many alterations for the seventh edition. One of the chief features is the space allotted to the applications in organic chemistry of physico-chemical methods such as refraction, absorption, viscosity, and so on. The importance of these properties in organic chemical research is steadily increasing, and I think it necessary to mention them even in a short text-book of this description. The chapter on carbohydrates has been modified by the inclusion of an account of the recent important researches of IRVINE, HAWORTH, and their collaborators on the constitution of the dioses, and by the rewriting of the section on enzymes. In connexion with dyestuffs a review of the relationship between constitution and colour is included. ROBINSON'S latest views as to the constitution of strychnine have been indicated. With a view to obviating undue expansion of the text as a result of the inclusion of new matter, I have deemed it imperative to sacrifice certain sections now of diminished importance. A comparison of this edition with the preceding issue will reveal numerous minor alterations in many parts of the volume.

When this book is read for the first time, the matter printed from small type should be omitted, as it contains numerous references to subsequent portions of the text. Such references are avoided in great measure in the part printed from large type.

A. F. HOLLEMAN.

BLOEMENDAAL, NETHERLANDS, July, 1930.

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AUTHOR'S PREFACE TO THE FIRST ENGLISH EDITION

Most of the short text-books of Organic Chemistry contain a great number of isolated facts; the number of compounds described in them is so considerable as to confuse the beginner. Moreover, the theoretical grounds on which this division of the science is based are often kept in the background; for example, the proofs given of the constitutional formulæ frequently leave much to be desired. However useful these books may be for reference, they are often ill-suited for text-books, as many students have learned from their own experience.

In this book I have endeavoured to keep the number of unconnected facts within as narrow limits as possible, and to give prominence to the theory underlying the subject. For this reason, a proof of the structure of most of the compounds is given. This was not possible for the higher substitution-products of the aromatic series, so that the methods of orientation employed in it are described in a special chapter.

Physico-chemical theories, such as the laws of equilibrium, ionization, and others, are becoming more and more prominent in organic chemistry. I have attempted in many instances to show how useful they are in this branch of the science. Such important technical processes as the manufacture of alcohol, cane-sugar, etc., are also included. The book is essentially a text-book, and makes no claim to be a "Beilstein" in a very compressed form.

Lastly, it may be mentioned that this book has also been translated into German, the second edition having just appeared, and that an Italian edition is in preparation.

A. F. Holleman.

Groningen, Netherlands, November, 1902.

NOTE

THE publication of this issue of Professor HOLLEMAN'S "Text-Book of Organic Chemistry" raises the total number of editions published in nine languages to fifty-two.

The text of the seventh English edition has been revised completely, and a considerable proportion of new matter has been incorporated.

Temperatures not marked specially are on the centigrade scale. References in the text to "Inorganic Chemistry" allude to the seventh English edition of Professor HOLLEMAN'S "Text-Book of Inorganic Chemistry," edited by Dr. HERMON C. COOPER, and published by Messrs. JOHN WILEY & SONS, INC. The "Laboratory Manual" mentioned is the fourth English edition of Professor HOLLEMAN'S "Laboratory Manual of Organic Chemistry for Beginners," published by Messrs. JOHN WILEY & SONS, INC. This work constitutes an appendix to the text-book, and should be employed as a guide to laboratory work prior to the systematic course of preparations essential to progress in the study of organic chemistry.

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ORGANIC CHEMISTRY.

INTRODUCTION.

1. Organic Chemistry is the Chemistry of the Carbon Compounds. The word "Organic" has now lost its historic meaning, given it at the beginning of last century, and originating in the belief in the impossibility of the formation of the animal and vegetable substances present in *organized* nature apart from an obscure and unique influence termed the "Vital force." At that time there was much confusion between organized substances, such as muscles, fibres, and other types of cells, and the true organic compounds constituting them. In his celebrated text-book published in the year 1831, BERZELIUS (1779–1848) emphasized the great improbability of such organic substances being prepared artificially, a conclusion induced mainly by this confusion of thought. Until almost the year 1850 the term "Organic Chemistry" was confined to the study of the compounds produced by plants and animals, and to that of the more or less complex decomposition-products obtainable from these substances by various means. Among these derivatives there were many not found in nature, but it was thought impossible to synthesize the compound bodies from their decomposition-products, or to obtain an organic compound from its elements.

Before this period isolated instances of the formation of organic compounds solely from inorganic material had been observed, the first synthesis of the type having been that of potassium cyanide from potassium carbonate, wood-charcoal, and ammonium chloride by SCHEELE in the year 1783. After a long interval of time, this discovery was followed by the synthesis by WÖHLER of oxalic acid in the year 1824 and of urea (**266**) in the year 1828, and later by that of acetic acid by KOLBE in the year 1845. These discoveries bore no fruit, being regarded as isolated instances unconnected with the main system of organic chemistry.

The great question of the synthesis of organic compounds from inorganic material was first tackled systematically by BERTHELOT with the objective of eliminating the idea of a "Vital force" from all explanations of organic chemical reaction. In his renowned work published in the year 1860, "La chimie organique fondée sur la synthese," he described a number of examples demonstrating the identity of the forces involved in the formation of both organic and inorganic compounds, and thereby engendered disbelief in the necessity for this purpose of any unique force.

The natural distinction between organic and inorganic chemistry having vanished, it was replaced by an artificial conception based on the known presence of carbon in all organic compounds, the name "Organic Chemistry" being allocated to the *Chemistry of the Carbon Compounds.*

The numerous discoveries made in the science, especially in Germany by LIEBIG, by WÖHLER, and by their pupils, and in France by DUMAS, by LAURENT, and by GERHARDT, imparted gradually to organic chemistry a wholly novel aspect, and eliminated the old division into groups of substances either with the same origin, as in vegetable chemistry or in animal chemistry, or with single properties in common, as exemplified by the vegetable acids, by the vegetable bases, and by neutral vegetable bodies. It was replaced by a more rational classification based on the mutual relationships found to exist between organic compounds, the form accepted at present being the product of gradual evolution.

2. Since there is no longer a clear line of demarcation between organic and inorganic chemistry, numerous syntheses having dissipated all doubt as to the theoretical possibility of building up from their elements even such complex carbon compounds as the proteins, the reasons for still treating the chemistry of the carbon compounds as a special part of the science demand an explanation. The basis for the convention is two-fold.

First, the enormous number of carbon compounds known, amounting to about two hundred and fifty thousand, that of the compounds of all the other elements being only about twenty-five thousand. Second, the unique nature of certain properties of the carbon compounds, either not found in the compounds of other elements, or at most in a much less marked degree. An example is the stability and resistance to chemical change displayed by many inorganic compounds at high temperatures, whereas almost all carbon compounds decompose at red heat. As a result, substances containing carbon are normally much less stable than inorganic products towards chemical and physical reagents, and the methods employed in the investigation of carbon compounds differ from those applicable to inorganic compounds.

Another peculiarity is the presence in numerous organic compounds of the same elements in the same proportions, although the substances display marked divergence in properties, exemplified by the existence of one hundred and thirty-five compounds of the formula $C_{10}OH_{13}O_2N$. This phenomenon is termed *isomerism*, and is almost unknown in inorganic chemistry, a fact necessitating consideration of its underlying cause.

All these reasons make it desirable to classify the carbon compounds as a special part of chemistry.

QUALITATIVE AND QUANTITATIVE ANALYSIS.

3. Lavoisier was the first to demonstrate the presence in most of the compounds of carbon of only a very small number of elements, the chief being *carbon*, *hydrogen*, *oxygen*, and *nitrogen*. *Halogen* derivatives are less numerous, and substances containing *sulphur* or *phosphorus* are still more rare. Carbon compounds having other elements also exist, but they are exceedingly few in comparison with those containing only the elements named. Some elements are not present in carbon compounds.

As a preliminary to determining the nature of a compound, the elements contained in it must be identified by *qualitative analysis*. For the carbon compounds this process involves oxidation, and is very simple in theory.

On solution of an organic compound, its constituent elements are usually not present in the liquid as ions. Oxidation either converts them at once into ions, or forms oxygen compounds with ionized groups such as CO_3'', SO_4'', and so on. They can then be identified by the ordinary inorganic reactions ("Laboratory Manual," I, 1–5).

Carbon is converted thus into carbon dioxide, detectible by the lime-water test; sulphur is oxidized to sulphuric acid and phosphorus to phosphoric acid; hydrogen is oxidized to water; and nitrogen is evolved in the free state.

If an organic compound contain a halogen, it is oxidized in presence of silver nitrate, the corresponding silver halide being formed. Any other elements present are converted by oxidation into compounds easily identified.

For analytical purposes, oxidation is effected by different methods, the choice being determined by the nature of the element suspected to be present. In testing for carbon, hydrogen, and nitrogen copper oxide finds general application. The substance is mixed with it, and the mixture is heated in a glass ignition-tube, the carbon and hydrogen being oxidized by the action of the oxygen of the copper oxide. Nitrogen is evolved in the free state, and can be recognized by the process involved in its quantitative estimation (7). With the halogens, sulphur, phosphorus, and other elements the best procedure is to oxidize the substance under examination with concentrated nitric acid.

The method of oxidation is of general applicability in qualitative analysis. It can be employed always, and yields positive results.

The desired end can be attained frequently with greater rapidity and facility by other methods; but as most of them are not of universal application, failure in detecting an element by one of them affords no certain indication of its absence. In doubtful instances the problem must be solved by the oxidation-process.

An example of the use of such limited methods is afforded by the possibility of detecting the presence of carbon in many compounds by submitting the substance to dry distillation. Charring often ensues, or there is evolution of vapours recognizable as carbon compounds by their smell, or by other properties such as burning with a smoky flame on ignition.

4. The nitrogen in many organic compounds can be converted into ammonia by heating them with soda-lime, or with concentrated sulphuric acid. Another method extensively employed in testing for this element was suggested by LASSAIGNE. It consists in heating the substance under examination with a small piece of sodium (or potassium) in a narrow ignition-tube. Should the compound contain nitrogen, sodium (or potassium) cyanide is formed, its presence being recognized readily by converting it into Prussian blue ("Laboratory Manual," I, 3, *a*).

5. The presence of halogens can be proved by heating the substance with quicklime, the corresponding calcium halide being formed. A very delicate method of detecting them is to introduce a small quantity of the compound on a piece of copper oxide into a non-luminous flame. The corresponding copper halide is formed and volatilizes, imparting a magnificent green colour to the flame. These two methods are always applicable.

Sulphur can be detected often by heating the compound with a small piece of sodium in a narrow ignition-tube. Sodium sulphide is produced, and can be identified by placing a portion of the reaction-mixture on a clean silver coin and adding water, a black stain of silver sulphide being formed. An alternative procedure is to extract the reaction-mixture with water and add sodium nitroprusside, the solution acquiring an intense violet colour.

No qualitative reaction for detecting oxygen in an organic compound is known. The operation can be effected by a quantitative analysis only.

6. The qualitative examination must be followed by a determination of the quantity of each element present in the compound, a process known as *quantitative analysis*. The methods of qualitative analysis in inorganic chemistry often are very different from those employed in quantitative determinations, but in organic chemistry the operations

of qualitative and quantitative analysis are alike in principle, oxidation being employed in both.

Carbon and hydrogen invariably are estimated simultaneously. The principle of the method of organic analysis chiefly employed is due to Liebig (1803–1873), the operation involving the following procedure. In the combustion-furnace, *k* (Fig. 1), is placed a hard-

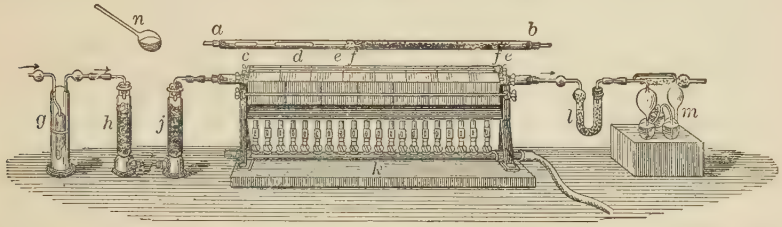


Fig. 1.—Organic Analysis.

glass tube *ab* open at both ends. A complete drawing of this tube is shown over the furnace in the illustration. It contains granulated copper oxide *ff*, and a roll of copper-gauze *c* oxidized by heating to redness in air or in a stream of oxygen. About one-third of the length of the tube is reserved for the introduction of a platinum or porcelain boat *d* containing a weighed quantity of the substance to be analysed. The insertion of the boat necessitates the temporary removal of the copper-gauze roll. The end of the tube next the boat is connected with an apparatus *ghj* to absorb water-vapour and carbon dioxide from the air or oxygen, *g* containing concentrated potassium hydroxide, *h* soda-lime, and *j* calcium chloride. To the end of the tube furthest from the boat is attached a weighed calcium-chloride tube *l*, for the purpose of collecting the water produced by the combustion of the substance. The weighed potash-bulbs *m* (shown enlarged in Fig. 2) are connected to this calcium-chloride tube, and in them the carbon dioxide formed is absorbed by concentrated potassium hydroxide. The gases enter the absorbers by the tube *b* on the right, pass through the three bulbs containing potassium hydroxide, and escape through the soda-lime tube *o*. After all the joints of the apparatus are known to be gas-tight, the burners are lighted, except beneath the boat. When the tube is hot, the substance is burned by heating this part of the tube carefully, at first a slow stream of air, and later a slow stream of oxygen, being led

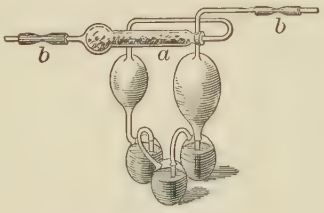


Fig. 2.—Potash-bulbs.

into the tube through the apparatus *ghj*. The oxygen facilitates the combustion of the deposited particles of carbon, and the red-hot copper oxide serves to oxidize the gaseous decomposition-products completely to carbon dioxide and water. The increase in weight of the calcium-chloride tube *l* gives the quantity of water formed, and that of the potash-bulbs *m* gives the quantity of carbon dioxide produced. From these data the amount of hydrogen and carbon in the compound can be calculated.

If the compound contain nitrogen or halogens, a freshly-reduced roll of copper-gauze is placed at the end of the tube nearest to the absorption-apparatus *l* and *m*. The hot copper decomposes any nitrogen oxides formed, and prevents their absorption in the potash-bulbs; it also retains the halogens as copper halides.

Methods of elementary microanalysis requiring only a few milligrammes of substance have been devised, mainly by PREGL.

7. Nitrogen is estimated usually by DUMAS's method. An apparatus similar to that employed in the estimation of carbon and hydrogen (Fig. 1) is used. The drying apparatus *ghj* is replaced by a carbon-dioxide KREUSSLER or KIPP generator, to effect complete expulsion of the air from the tube prior to the combustion. For the absorption-apparatus *lm* is substituted a delivery-tube opening under mercury. The air having been expelled from the apparatus, the front part of the tube containing the copper-gauze and the granulated copper oxide is heated. The combustion is then begun, and the evolved gases are collected in a graduated tube open at the bottom (measuring tube), with its open end dipping into the mercury-bath. This tube is filled partly with mercury, and partly with concentrated potassium-hydroxide solution to absorb the carbon dioxide. The reduced copper-gauze decomposes any nitrogen oxides formed. The combustion being over, all the nitrogen remaining in the combustion-tube is swept into the graduated tube by a stream of carbon dioxide from the KREUSSLER or KIPP generator. The measuring tube containing the mercury, potassium-hydroxide solution, and gas is introduced into a wide cylinder filled with water. The mercury and potassium-hydroxide solution are displaced by the water, and after the level of the liquid inside the tube has been made to coincide with that outside, the number of cubic centimètres of nitrogen is noted. From the reading the amount of nitrogen in the compound is calculated.

Nitrogen often can be estimated by a method discovered by KJEL-

DAHL and improved by WILFARTH. It depends on the possibility of converting completely into ammonia the nitrogen of many organic substances by heating such compounds for a time with concentrated sulphuric acid in presence of phosphoric oxide and a drop of mercury, the metal going into solution. Owing to charring, the mixture usually blackens at first, but after heating for one or two hours it becomes quite colourless. At this stage, the carbon has undergone complete oxidation by the oxygen of the sulphuric acid, a reaction attended by reduction to sulphurous acid. The process is facilitated by the mercury salt, it probably playing the part of an " Oxygen-carrier " between the sulphuric acid and the organic substance, and being converted continually from the mercuric to the mercurous state, and then by the boiling acid back into the mercuric state. When the liquid has become colourless, it is allowed to cool and is diluted with water; excess of alkali is added, and the ammonia is expelled by heat into a measured quantity of acid of known strength. Titration gives the quantity of ammonia, and hence the amount of nitrogen. This neat and simple method usually is not applicable to compounds containing oxygen in union with nitrogen. With such compounds the conversion of nitrogen into ammonia is only partial.

8. The halogens can be estimated either by the method of LIEBIG or by that of CARIUS. In LIEBIG'S process the substance is heated with quicklime, and in that of CARIUS with a small quantity of concentrated nitric acid and a crystal of silver nitrate in a sealed glass tube at a high temperature. CARIUS'S process is operated without risk in the tube-furnace (Fig. 3), the glass tubes being placed in wrought-iron cylinders with thick walls.

CARIUS'S method can be applied also to the estimation of sulphur, phosphorus, and other elements. Non-volatile substances containing sulphur or phosphorus can be oxidized also by fusion with nitre.

For the quantitative estimation of nitrogen and the halogens TER MEULEN has recently devised new methods based on a wholly different principle, and giving accurate results quickly. For nitrogen the substance is mixed with finely divided nickel-powder, and heated in a current of hydrogen. The mixture of the evolved gases with hydrogen is passed over asbestos coated with nickel-powder. By this means the nitrogen is converted quantitatively into ammonia, the amount of this product being determined by titration.

The method of TER MEULEN and HESLINGA for the estimation of halogens involves heating the substance in a mixture of hydrogen and gaseous ammonia. There is a quantitative formation of ammonium halide, and the amount of halogen can be ascertained by titration.

9. The results of a quantitative analysis are expressed in percentage-numbers. If the total of these percentage-numbers be very nearly 100,

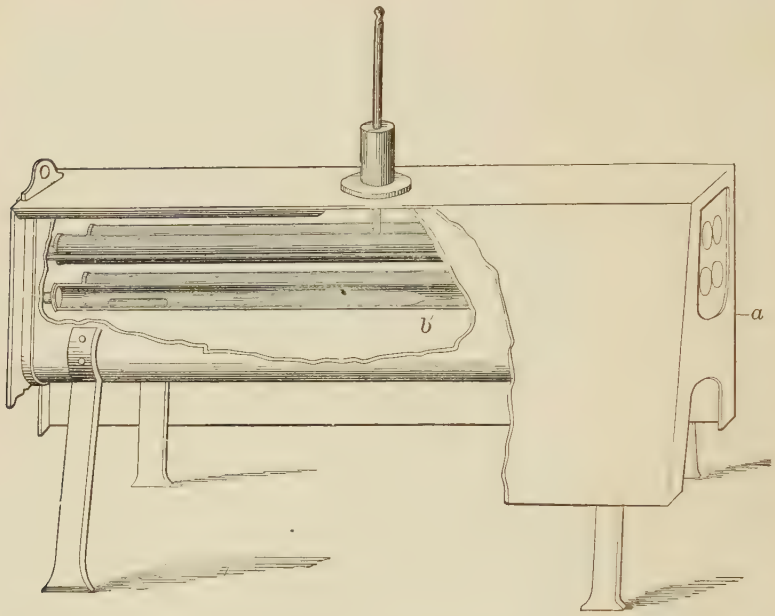


FIG. 3.—TUBE-FURNACE.

no other element is present in the compound; but if appreciably less than 100, there is present another element outside the scope of the analysis, there being no convenient method for its estimation. This element is *oxygen*. The percentage-amount of oxygen must be determined by subtracting the total of the percentages of the other elements from 100. This method has the disadvantage of including all experimental errors in the percentage-number of the oxygen.

Owing to the loss of a small proportion of carbon dioxide through the various connexions of the apparatus, carbon-estimations are normally too low. Hydrogen-estimations are generally too high, because copper oxide is hygroscopic, and cannot be freed readily from traces of moisture. To some extent these errors balance, the inaccuracy of the oxygen-percentage being diminished proportionately.

The method of calculating from the results of analysis the percentage-composition and formula of a substance is explained most readily by means of an example.

The analysis of a substance containing nitrogen yielded the following numbers:

0·2169 g. substance gave 0·5170 g. of carbon dioxide and 0·0685 g. of water.

0·2218 g. substance gave 17·4 c.c. of nitrogen, measured over water at 6° C. and 762 mm. barometric pressure.

Since there are 12 parts by weight of carbon in 44 parts by weight of carbon dioxide, and 2 parts by weight of hydrogen in 18 parts by weight of water, the weight of the carbon dioxide formed must be multiplied by $\frac{12}{44}=\frac{3}{11}$ to find the weight of carbon, and that of the water produced by $\frac{2}{18}=\frac{1}{9}$ to obtain the weight of hydrogen. This calculation gives 65·0 per cent. of carbon and 3·51 per cent. of hydrogen in the compound.

The weight of the nitrogen is calculated as follows. Since the gas is saturated with water-vapour, to obtain the true pressure of the nitrogen the tension of this vapour expressed in millimètres of mercury must be subtracted from the barometric pressure. At 6° C. the tension of aqueous vapour is 7·0 mm. The actual pressure of the nitrogen is therefore 762−7=755 mm. Since 1 c.c. of nitrogen at 0° and 760 mm. weighs 1·2562 mg., at 755 mm. and 6° C. the weight in milligrammes of this volume is

$$\frac{1\cdot2562}{1+6\times0\cdot00367}\times\frac{755}{760}=1\cdot2211.$$

Since the 17·4 c.c. of nitrogen obtained weigh

$$1\cdot2211\times17\cdot4=21\cdot247 \text{ mg.},$$

the percentage of nitrogen is 9·6.

The sum of these percentage-numbers being 78·1, the percentage of oxygen in the substance analysed is 21·9. The percentage-composition given by the analysis is therefore

C=65·0
H= 3·5
N= 9·6
O=21·9.

Division of these values by the numbers representing the atomic weights of the corresponding elements gives

C	H	N	O
5·4	3·5	0·7	1·4.

These numbers divided by 0·7 give the quotients

C	H	N	O
7·7	5·0	1·0	2·0.

These quotients approximate very closely to those required by the formula $C_8H_5O_2N$. The percentage-compositions corresponding with this formula are

$$C=65\cdot3, \qquad H=3\cdot4, \qquad N=9\cdot5,$$

in good accord with the analysis.

DETERMINATION OF MOLECULAR WEIGHT.

10. Analysis gives only the empirical formula of a compound, and not its molecular formula, $C_aH_bO_c$ having the same percentage-composition as $(C_aH_bO_c)_n$. The empirical formula having been ascertained by analysis, the *molecular weight* has still to be determined.

Its value cannot be decided by chemical means, although it is possible thus to assign a minimum to the molecular weight. An example is furnished by the empirical formula of benzene, CH. Benzene yields readily a compound C_6H_5Br, reducible again to benzene. It follows that the molecule of benzene must be represented by C_6H_6 at least. The molecular formula could also be $C_{12}H_{12}$, or, in general, $(C_6H_6)_n$; the bromine compound would then have the general formula $(C_6H_5Br)_n$. Assuming the formula to be $C_{12}H_{12}$, that of the bromine compound would be $C_{12}H_{10}Br_2$. Obviously the formation of a compound of this formula would involve direct replacement of two hydrogen atoms by bromine, and the next step would be to experiment with the object of obtaining a substance of the formula $C_{12}H_{11}Br$. Should the experiments fail, the probability of the accuracy of the simpler formula C_6H_5Br would be increased. The indications thus afforded would not be decisive, because the experimental conditions necessary to the formation of the compound $C_{12}H_{11}Br$ might not have been attained. The chemical method proves the molecular formula of benzene not be smaller than C_6H_6, but does not exclude the possibility of a multiple of this formula.

To ascertain the true molecular weight, physical methods must be employed. They involve the determination either of the density of the compound in the gaseous state, or of certain values dependent on the osmotic pressure of the substance in dilute solution. The theory of

these methods being explained fully in "Inorganic Chemistry," 31–35 and 40–45, it will suffice to describe the practical details of a molecular-weight determination.

In calculating the *vapour-density* (the density of the substance in the gaseous state), four quantities must be known; the weight of substance converted into the gaseous state, the volume of the resulting vapour, the temperature of measurement, and the barometric pressure.

11. Vapour-density is determined usually by a method suggested by Victor Meyer. The apparatus (Fig. 4) consists of a glass tube *B* with an internal diameter of about 4 mm. This tube is closed at the top with a stopper, and underneath has a wider cylindrical portion of about 200 c.c. capacity, closed at the lower end. Near the top of the tube is sealed on a delivery-tube *A* for passage of the gas prior to collection over water in the graduated tube *E*. The apparatus is surrounded partly by a wide glass or metal jacket *C* containing a liquid boiling higher than the substance under investigation. This liquid is heated to boiling, some of the air in *B* undergoing expulsion. After the lapse of a short period of time no more air escapes from the delivery-tube, that in the wider part of the tube having a constant temperature almost equal to that of the vapour of the boiling liquid. The graduated tube is filled with water and placed over the open end of the delivery-tube *A*. After the stopper has been withdrawn, a weighed quantity of the substance under examination enclosed in a small glass tube is dropped into the apparatus, and the stopper replaced, care being taken to make it air-tight. The substance vaporizes quickly in the heated wide portion of the tube, its vapour expelling air from the apparatus. The air is collected in the graduated tube, its volume being equal to that of the vapour. Although the air in the hot part of the apparatus has the local temperature, that in the graduated tube acquires the temperature of this tube, a factor in the calculation. The volume noted is equal to that which the weighed portion of the substance in the form of vapour would occupy, if it were possible to

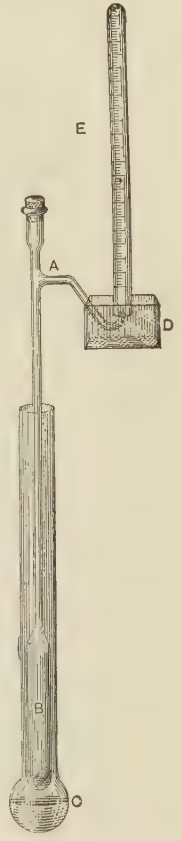


Fig. 4.—Victor Meyer's Vapour-density Apparatus.

convert it into a gas at the ordinary temperature and under the barometric pressure.

For ease of manipulation this method leaves nothing to be desired. It possesses an additional great advantage over the other methods, a knowledge of the temperature of the apparatus being unnecessary for the calculation. It is only requisite for the temperature to remain constant during the short time occupied by the experiment.

An example will make the method of calculation clear. Suppose g mg. of the substance to have been taken, and to have yielded V c.c. of air measured over water with the level the same inside and outside the tube; suppose further the barometric pressure to be H, the temperature t, and the tension of aqueous vapour b; then, at a pressure of $H-b$ mm. and at $t°$, g mg. of the substance would occupy a volume of V c.c., and under these conditions the unit of volume (1 c.c.) would contains $\frac{g}{V}$ mg. of the substance.

One cubic centimètre of oxygen at $H-b$ mm. of pressure and at $t°$ weighs in milligrammes

$$\frac{1\cdot429}{1+0\cdot00367t}\times\frac{H-b}{760},$$

giving for the vapour-density D referred to oxygen = 16 the expression

$$D=16\frac{g}{V}\times\frac{1+0\cdot00367t}{1\cdot429}\times\frac{760}{H-b}.$$

The molecular weight M being twice the density,

$$M=2D.$$

12. Two other methods are employed often in ascertaining the molecular weights of organic compounds. They are based on the laws of osmotic pressure, and involve the determination of the depression of the freezing-point or the elevation of the boiling-point of a dilute solution of the substance, referred to either the freezing-point or the boiling-point of the pure solvent ("Inorganic Chemistry," 40–45).

In the depression method it is necessary to determine first the freezing-point of the solvent; for example, that of phenol. Then one gramme-molecule of a substance of known molecular weight is dissolved in a known weight of the solvent. The volume of the solvent can be calculated from its weight.

The solute lowers the freezing-point by an amount always the same for the same solvent, and independent of the nature of the substance

provided the volume of solution containing one gramme-molecule is the same. The depression of the freezing-point caused by a gramme-molecule is accordingly a constant for this solvent. If a solution of one per cent. strength of a substance of unknown molecular weight M be made in phenol, and the resultant depression (A) of the freezing-point determined, then

$$AM = \text{Constant};$$

because between certain limits the depression of the freezing-point is proportional to the concentration.

Obviously this formula is equally applicable to the elevation of the boiling-point. M is the only unknown quantity, and can be calculated from the equation.

The product AM is termed the *molecular depression of the freezing-point* or the *molecular elevation of the boiling-point* of the solvent.

Examples.—Numerous determinations with phenol as solvent having proved the molecular depression of its freezing-point to be equal to 75, for this solvent

$$AM = 75.$$

A solution of 2·75 per cent. concentration was prepared by dissolving 0·3943 g. of a substance of empirical formula $C_7H_7ON_2$ in 14·34 g. of phenol. The depression of the freezing-point of this solution was 0·712°. For a solution of one per cent. strength the depression would have been $\frac{0·712}{2·75} = 0·258$, therefore $A = 0·258$. The molecular weight is accordingly $\frac{75}{0·253} = 291$.

$C_7H_7ON_2$ corresponds with the molecular weight 135, and $C_{14}H_{14}O_2N_4$ with 270, the higher number approximating more closely to the molecular weight found. The molecular formula of the compound is obtained by doubling the empirical formula.

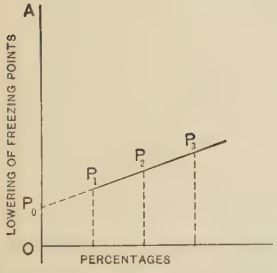


Fig. 5.—Eykman's Graphic Method.

The laws of osmotic pressure hold only for very dilute solutions. This qualification applies also to the equation $AM = \text{Const.}$, since it is derived from these laws.

It is not strictly correct to determine A by means of a solution of finite concentration, as is done in the example given. To determine M accurately, the value of A should be derived from a solution of infinite dilution; but as this process is not possible, Eykman has devised a *graphic method* of finding A for such a solution. A is determined for

three or four concentrations, and the values obtained are represented graphically as in Fig. 5, the values of A being the ordinates, and those of the percentage-strengths of the solutions being the abscissæ. Frequently EYKMAN found the line drawn through the tops of the ordinates to be almost straight. If it be produced until it cuts the ordinate OA, OP_0 gives the value of A for infinite dilution.

13. The constants for the *molecular depression of the freezing-point* of a number of solvents are given in the table.

Solvent.	Melting-point.	Molecular Depression.	
		Observed.	Calculated.
Water	0°	19	18·9
Acetic acid	16·5°	39	38·8
Benzene	6°	53	53
Nitrobenzene	5°	70	69·5
Phenol	39·6°	75	77
Naphthalene	80°	69	69·4
Urethane	48·7°	51·4	—
Stearic acid	53°	45	—
p-Toluidine	42·5°	52·4	—
Camphor	174°	400	—

The last five solvents are very useful, and not being hygroscopic are better than the glacial acetic acid still often employed. The fact of their melting above the ordinary temperature so as to eliminate the necessity for a cooling agent, and the high value of their constants, are additional advantages.

Camphor is specially distinguished in these respects, and does not require the use of a thermometer graduated in tenths of a degree. Its molecular depression is so great as to render an ordinary thermometer applicable.

The following table indicates the *molecular elevations of the boiling-point* usually to be smaller than the molecular depressions of the freezing-point.

Solvent.	Boiling-point.	Molecular Elevation.	
		Observed.	Calculated.
Water	100°	5·1	5·2
Ether	35·6°	22·1	21·1
Ethyl alcohol	78·0°	11·3	11·5
Benzene	80·4°	26·0	26·7
Chloroform	61·0°	35·6	36·6
Acetone	56·3°	17·3	16·7

The numbers in the last column of the tables are calculated from VAN 'T HOFF's formula

$$K = \frac{0{\cdot}02 \times T^2}{W},$$

K being the molecular depression or elevation, T the freezing-point or boiling-point on the absolute scale, and W the latent heat of fusion or of evaporation per kilogramme of the solvent.

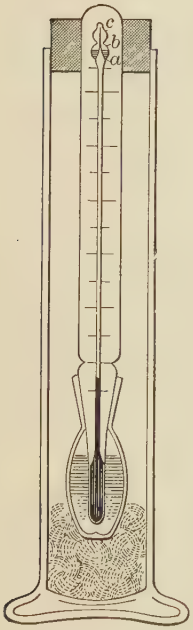


FIG. 6.—EYKMAN'S DEPRESSIMETER.

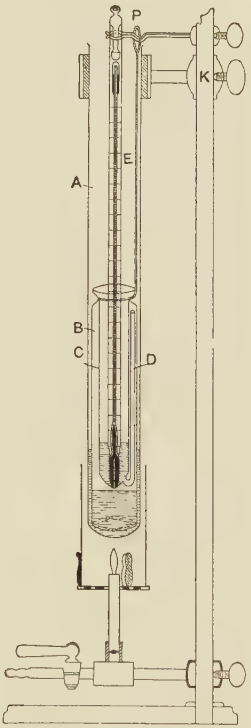


FIG. 7.—EYKMAN'S BOILING-POINT APPARATUS.

14. EYKMAN has constructed convenient apparatuses for the determination of the depression of the freezing-point and the elevation of the boiling-point. The depressimeter (Fig. 6) comprises a short thermometer divided into twentieths of a degree with a small flask attached as shown in the figure, this combination being contained in a glass cylinder held at the top by a stopper, and supported underneath by cotton-wool. Being a poor conductor of heat, the cotton-wool

retards cooling. A weighed quantity of the solvent is placed in the flask, and its freezing-point is determined. Then a known weight of the substance is introduced, and the freezing-point is observed again. From the depression of the freezing-point thus obtained A can be calculated as in the example given (12).

15. Eykman's apparatus (Fig. 7) for determining the elevation of the boiling-point comprises a thermometer, and two glass vessels A and B. The tube A is about 40 cm. long and 4 cm. wide, and serves both as a heating jacket for the pure solvent, and as an air-condenser. B is only a few millimètres narrower than A, and to it is fused the boiling-tube C with a narrow side-tube D. C is suspended by the neck from the clamp K by a platinum wire P, and can be raised or lowered at will. The thermometer-scale is divided into tenths of a degree, the graduations being about one millimètre apart, so that with the aid of a lens it is possible to read to one-hundredth of a degree. Besides giving the boiling-point, the graduated scale of the thermometer also serves to indicate the volume of solution contained in C. For this purpose the vessel C with the thermometer placed in it must be calibrated by a gravimetric or volumetric method.

When using the apparatus the solvent is introduced into C until the level of the liquid has risen to that of the first graduation on the thermometer-scale, between 5 and 10 c.c. being needed. About 40 or 50 c.c. of the solvent are poured into the jacket A, and the apparatus is heated with a micro-burner, using a large flame at first. When ebullition has begun, the size of the flame is reduced so as to cause complete condensation of the vapour in the tube A at a height shown in the figure by the letters A or E.

When the liquid has boiled at a constant temperature for a short time, the height of the mercury is noted, and the clamp is raised so as to bring the level of the open end of the boiling-tube C to a position some centimètres above the top of the jacket A. A weighed quantity, about 1 or 2 milligramme-molecules, of the substance under investigation is then introduced into C from a tared weighing-tube, and C is lowered gently to its former position in the jacket. While the weighing-tube is being weighed to ascertain the quantity of substance added, the boiling-point of the solvent will have become constant. This temperature is noted, the boiling-tube C is raised again by the aid of the clamp K, and the volume is determined accurately by reading with a lens the height of the solution-meniscus on the thermometer-scale.

A second determination is made with a solution of greater concentration by introducing a further quantity of the substance from the

weighing-tube, and repeating the series of operations just described. Since very little more time is needed for each operation than is required to tare the weighing-tube and its contents, a series of determinations at different concentrations can be made quickly, and the results plotted on squared paper. From the curve thus obtained the value of A for infinite dilution can be calculated readily (**12**).

THE ELEMENT CARBON.

16. Carbon has three allotropic forms, *diamond*, *graphite*, and *amorphous carbon*. For a description of them and of the compounds of carbon with metalloids and with metals, as well as of the determination of its atomic weight and molecular weight, reference should be made to "Inorganic Chemistry," **173–177**. The evidence in favour of assuming the molecule of carbon to contain a great number of atoms is set forth there.

Confirmation of this view is afforded by a consideration of the relationship between the boiling-points of the compounds of carbon and of hydrogen. If these derivatives be assigned the general formula C_nH_{2n-p}, then, even when both n and p are large numbers, the boiling-points of these substances are relatively low, and rise with the increase of both n and p. For carbon itself $2n=p$, and on account of the extraordinary non-volatility of this substance the value of n must be very great.

The subject of *valency* is explained in "Inorganic Chemistry," **76**. With univalent elements carbon forms compounds of the type CX_4. *It is therefore quadrivalent, and on this foundation the whole superstructure of organic chemistry rests.*

LABORATORY METHODS.

17. To prevent repetition, it is desirable before proceeding with a description of the organic compounds to give a short account of the more important operations employed in their preparation and investigation.

Heating Mixtures of Substances.—This process is used very often to induce reaction between bodies, the velocity of reactions increasing markedly with rise of temperature ("Inorganic Chemistry," **13** and **104**). The details vary according to the temperature to be attained.

If this temperature be considerably below the boiling-point of the most volatile compound, the substances are mixed together in a flask fitted with a thermometer, as in Fig. 8. The flask is immersed in an air-bath formed of a vertical iron cylinder closed at the lower end, a piece of stove-pipe being very suitable. The upper end is closed with a sheet of asbestos mill-board, with an opening for the neck of the flask. Should the boiling-point of one of the substances be reached or overstepped, the flask must be connected with a condenser, as in Fig. 9. The invention of this form of condensing apparatus is attributed usually to LIEBIG, although it was constructed first in 1771 by WEIGEL. It consists of a glass tube *aa*, enclosed in

FIG. 8. — HEATING SUBSTANCES IN AN OPEN FLASK.

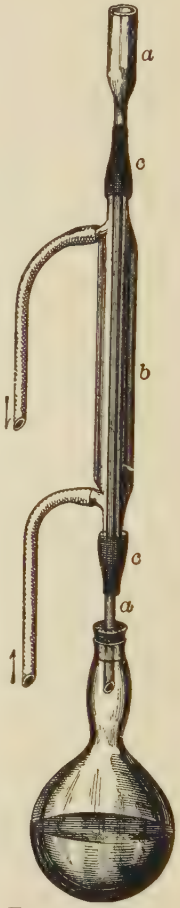


FIG. 9. — FLASK WITH REFLUX-CONDENSER.

a jacket *b* of glass or metal with a current of cold water circulating. For substances of high boiling-point a plain vertical glass tube can be substituted; it is termed an "air-condenser," being sufficiently cooled by the air alone. The effect of the condenser is to condense the vapour of the boiling material, and to direct the liquid back into the flask. When a substance has to be heated above its boiling-point, it is placed in a thick-walled glass tube sealed at one end, and after the

open end has been sealed the tube is heated in a tube-furnace (9, Fig. 3).

18. *Distillation.* — The apparatus shown in Fig. 10 may be

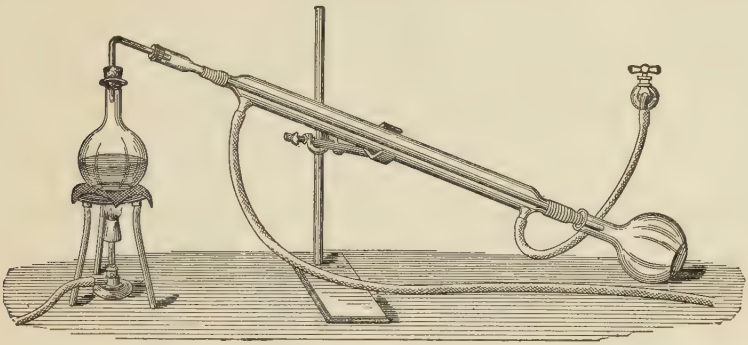


Fig. 10.—Distillation-apparatus.

employed for distillation, but if the liquid to be distilled be of such a nature as to induce contamination through the action of its vapour on the cork or rubber stopper shown in the figure, a distilling-flask (Fig. 11) is substituted. If the neck of this flask be of sufficient length, contact of the vapour with the stopper during distillation is prevented.

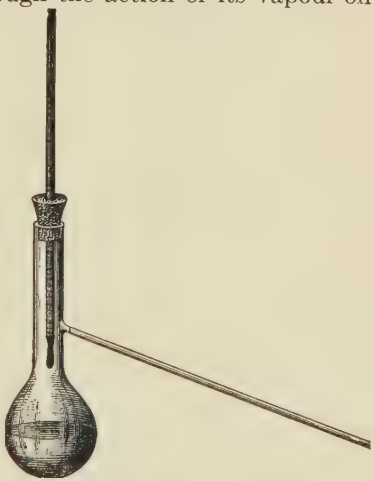


Fig. 11.—Fractionating-flask.

On heating to their boiling-points at the ordinary pressure many substances decompose, but under diminished pressure distil unchanged, because the boiling-point is then much lower. The apparatus shown in Fig. 12 can be utilized for vacuum-distillation.

The liquid for distillation is placed in *d*. A glass tube *e*, drawn out to a very fine point, dips into the liquid, and a thermometer is placed in this tube. When the apparatus has been evacuated by the water-pump *w*, a stream of minute bubbles of air escaping from the fine point of the tube *e* serves to prevent the violent "bumping" otherwise characteristic of liquids boiling under diminished pressure. This bumping is due to the sudden and intermittent formation of vapour, and sometimes causes boiling over or the fracture of the flask. The

receiver *b* is kept cool by a stream of water from *c*. The part *m* is a mercury manometer; *a* is a two-way stop-cock permitting access of air to the apparatus after the distillation, and also serving to disconnect the water-pump from the rest of the system should the pump "strike back." By this means rise of water into the manometer and the flasks through the tube *s* can be obviated.

19. The separation of a mixture of volatile substances is effected by *fractional distillation*. If a mixture of two liquids, boiling for example at 100° and at 130°, be distilled, a greater proportion of that boiling at 100° distils over at the beginning of the operation, and a greater proportion of that boiling at 130° at the end. If the distillate

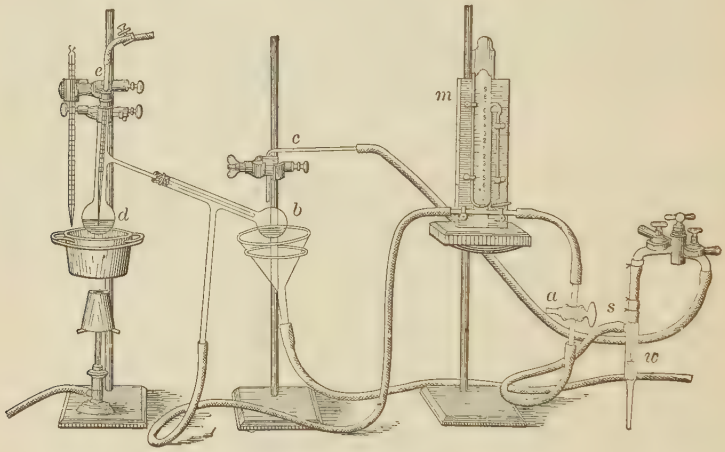


FIG. 12.—DISTILLATION IN VACUUM.

passing over below 110° be collected separately in one fraction, and similarly that between 120° and 130°, a rough separation is attained, whilst the middle fraction still consists of a mixture. To make the separation as complete as possible, the fraction between 100° and 110° is returned to the fractionation-flask and distilled until the thermometer reaches 110°, the fraction between 110° and 120° being then mixed with the residue in the fractionation-flask, and the distillation continued until the thermometer stands again at 110°. The receiver is changed, and the distillation is renewed until the thermometer reaches 120°. The fraction between 120° and 130° is then added to the liquid in the distillation-flask, and the distillate is collected in the same receiver until the thermometer indicates again 120°. The portion distilling subsequently is collected separately. By several repetitions of this process it is possible often to effect an almost complete separation, it being

usually advantageous to collect the fractions between narrower limits of temperature, and thus to increase their number.

20. The separation is much facilitated by employing a fractionating-column (Fig. 13) connected to the neck of the boiling-flask, a large proportion of the vapour of the least volatile constituents of the mixture becoming condensed in the column. The stream of vapour from the

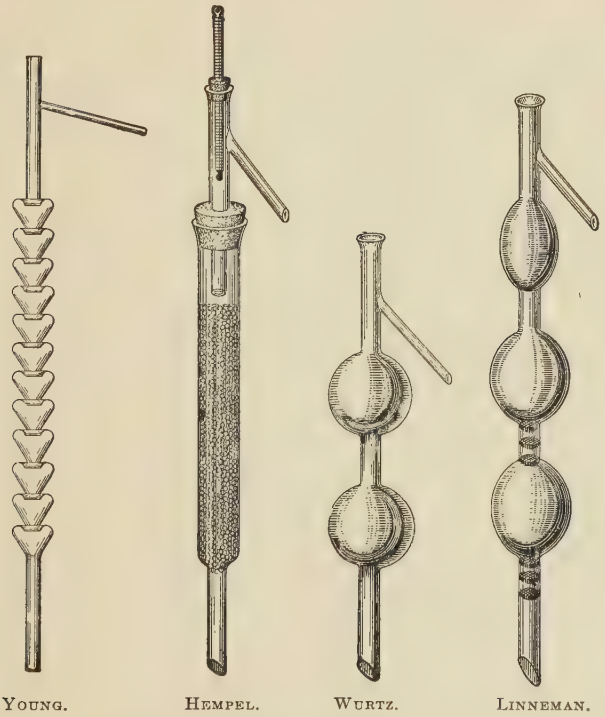


Fig. 13.—Fractionating-columns.

distillation-flask heats the liquid thus formed in the fractionating-column, the effect being to vaporize its more volatile part, and simultaneously to condense the higher-boiling constituent of the vapour issuing from the flask.

21. A change in the composition of most liquid mixtures does not occasion a proportional alteration in their properties, like that expressed by the straight line AB in the annexed graphic representation (Fig. 14). The abscissæ correspond with the molecular percentage-composition of the mixtures. The points A and B on the ordinates give the values of such physical constants as vapour-tension, boiling-point, density, and so

on, for the pure substances A and B, and the line AB the values of these constants for mixtures. The curve thus obtained usually varies somewhat from a straight line.

The boiling-points of mixtures will be lower (line c) or higher (line b) than those calculated by the proportion-rule. Sometimes these boiling-point curves will depart so much from the straight line as to show such maxima and minima as the curves a and d. Complete separation of such

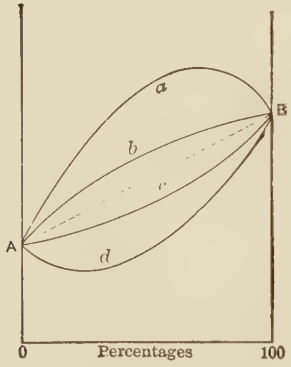


Fig. 14.

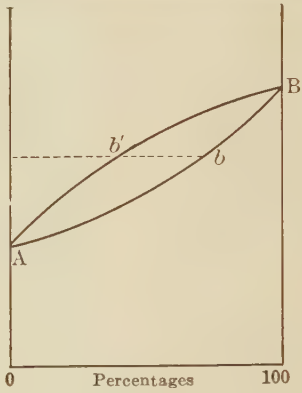


Fig. 15.

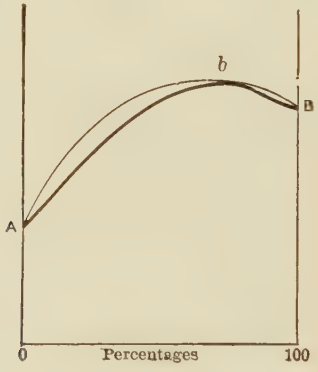


Fig. 16.

Fractional-distillation Curves.

mixtures by fractional distillation at constant pressure is impossible, but is feasible when the boiling-point curves follow the course indicated by b or c. The most volatile, or lowest boiling, constituent of a mixture always distils first, so that the vapour is richer in A and the residual liquid in B. If the pure constituents A and B be more, or less, volatile than any mixture of the two, as represented by the boiling-point curves b and c, continued fractional distillation must lead to an approximately complete separation of A and B. But if the boiling-point curve have a maximum or minimum,

the mixtures corresponding with it will consist of the most, or least, volatile constituents. On distillation, a fraction with this highest, or lowest, boiling-point will be obtained always, and at constant pressure further separation will be impossible.

Comprehension of this phenomenon will be facilitated by considering a boiling-point curve b without a maximum or minimum (Fig. 15). Since the most volatile portion of any mixture always volatilizes first, the vapour evolved from a boiling liquid always contains a greater proportion of A than the liquid itself. When the composition of the mixture is b, that of the liquid will be b'. The *vapour-tension curve* $Ab'B$ throughout the complete trajectory AB lies higher than the boiling-point curve.

If the boiling-point curve have a maximum b (Fig. 16), along the trajectory Ab the vapour will be richer in A than the parent liquid; along the trajectory bB the vapour will contain a greater proportion of B than the parent liquid, B being now the most volatile, or lowest boiling, constituent. Consequently at the maximum b the composition of the vapour must be identical with that of the liquid, and the mixture with maximum boiling-point distils at a constant temperature as though it were a single substance. For a mixture of liquids with a minimum boiling-point analogous results are obtained, so that in the graphic representation the vapour-tension curve must be tangential to the boiling-point curve, and touch it at the minimum-point.

The separation of a mixture of liquids by fractionation is also impossible when the boiling-points of its constituents are close together, because the essential characteristic of the whole method consists in the unequal volatility of the portions composing the mixture, resulting in the distillation of one substance before the other. If the substances have nearly the same boiling-point, then both attain a vapour-tension of one atmosphere at almost the same temperature; in other words, they are almost equally volatile. With these conditions it is therefore impossible to apply the method successfully.

22. *Steam-distillation.*—In the preparation of many organic substances a crude reaction-product containing tarry matter is produced frequently along with the required compound. To free the substance from this contamination, use is made often very advantageously of the property possessed by many substances of distilling in a current of steam, the tarry matter remaining behind. Fig. 17 shows the apparatus employed in such a distillation.

Water is boiled in the can a, fitted with a delivery-tube c and a safety-tube b, the evolved steam being passed into the bottom of the distillation-flask d. If the distillation be interrupted, cooling causes diminished pressure in a, air being then able to enter the tube b. If b were not used, the liquid in d would flow back into a owing to the fall in the steam-pressure.

Steam-distillation is also of service in separating compounds volatile in steam from others not volatile in it. With substances insoluble in water the distillate is a milk-like liquid, because the water in the receiver

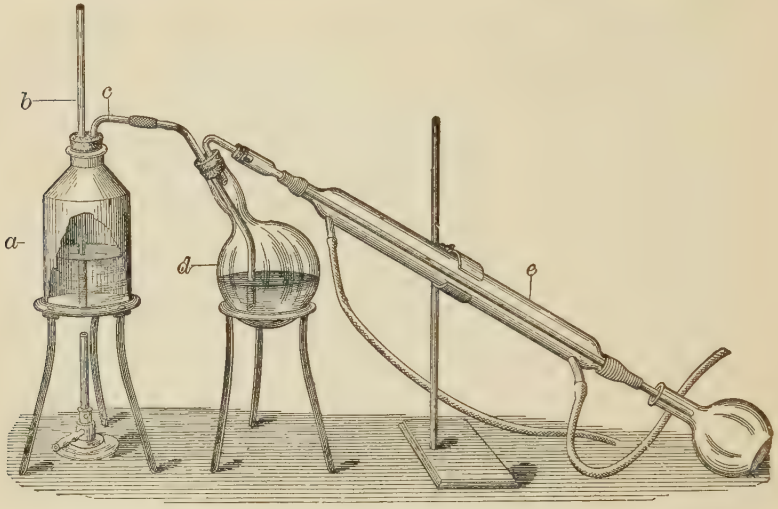


FIG. 17.—STEAM-DISTILLATION.

is mixed with fine oily drops. There is also an oily layer above or below the water.

In steam-distillations two liquids take part, water and the substance to be distilled. Usually these liquids are not miscible in all proportions. In the limiting case of each liquid being wholly insoluble in the other, the vapour-pressure of each is unaffected by the presence of the other. Since the liquid is boiling, the sum of the vapour-pressures of the two constituents at the boiling-point of the mixture must be equal to the barometric pressure. The boiling-point must be lower than that at ordinary pressure of the lower-boiling of the two substances, because the partial pressure is necessarily smaller than the total pressure, which is equal to that of the atmosphere. The same result is therefore attained as by distillation at diminished pressure, the volatilization of the substance being effected at a temperature lower than its boiling-point under ordinary pressure.

The velocity of distillation of a substance in steam depends on its partial pressure and on its vapour-density, and also on the values of these physical constants for water. If the pressures be p_1 and p_2, and the vapour-densities d_1 and d_2, the quantities distilling simultaneously are p_1d_1 (substance) and p_2d_2 (water). If the ratio $p_1d_1 : p_2d_2$ be large, the substance distils with a small quantity of water, the distillation being completed quickly. The converse holds for a ratio $p_1d_1 : p_2d_2$ of small magnitude.

At a pressure of 760 mm. a mixture of nitrobenzene and water boils at 99°. The steam exerts a pressure of 733 mm., so that the tension of the nitrobenzene-vapour is 27 mm. Since the vapour-densities of water and nitrobenzene are in the ratio of their respective molecular weights, 18 and 123, the proportion of water to nitrobenzene in the distillate should be as $733 \times 18 : 27 \times 123$; that is, approximately as 4 : 1. Notwithstanding its small vapour-tension at the boiling-point of the mixture, the quantity of nitrobenzene collected is about one-fifth of the total distillate, the rapid volatilization of the nitrobenzene being due to its molecular weight being large compared with that of water. Even when an organic compound under similar conditions has a vapour-tension of only 10 mm., it distils in steam with sufficient rapidity to render the method applicable to its purification.

23. *Separation of Two Immiscible Liquids.*—For separating two immiscible liquids a *separating-funnel* (Fig. 18) is employed, the drawing indicating the procedure without further explanation. The method is applied also to the *extraction* of aqueous solutions of substances soluble in a volatile liquid immiscible with water, such as *ether*, *light petroleum*, *chloroform*, and *carbon disulphide*. The solution is transferred to a separating-funnel, the solvent selected is added, and after the mouth of the funnel has been closed by a glass stopper the two liquids are mixed by vigorous agitation, whereupon the substance dissolved in the water passes partly into the solvent. When ether has been selected for the extraction, the ethereal solution is allowed to rise to the surface, and separated from the water by opening the stop-cock after removal of the stopper. The water dissolved by the ether during the agitation is removed by chloride of calcium or some other desiccator, and finally the ether is distilled. When the dissolved substance is only slightly soluble in water and readily soluble in ether, the extraction is completed quickly, it being then possible to exhaust the aqueous solution almost completely by several repetitions of the process, separate portions of ether being employed for each extraction. Otherwise, frequent repetitions of the agitation are necessary, and even then the extraction is imperfect.

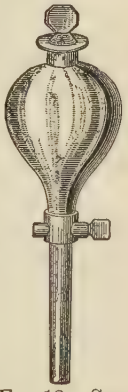


Fig. 18.—Separating-funnel.

In accordance with the law of Berthelot, when two immiscible solvents are in contact simultaneously with a substance soluble in both, the solute distributes itself so as to establish a constant ratio between the concentrations attained in the solvents. If a quantity X_0 of the substance be dissolved in a quantity l of the first solvent (water), and this solution be extracted with a quantity m of the second solvent (ether), there will then

remain a quantity X_1 in the first solution, so that $X_0 - X_1$ has passed into the second solvent.

In accordance with the law cited, the value of the quantity X_1 is given by the equation

$$\frac{X_1}{l} = K\frac{X_0 - X_1}{m} \quad \text{or} \quad X_1 = {}_0X\frac{Kl}{m+Kl},$$

for $\frac{X_1}{l}$ and $\frac{X_0 - X_1}{m}$ are the two concentrations after agitation with the solvents, and K is the number expressing the constant ratio, or the *coefficient of distribution*.

A second extraction with the same quantity m of the second solvent gives

$$\frac{X_2}{l} = K\frac{X_1 - X_2}{m},$$

or, substituting the value of X_1 from the first equation,

$$X_2 = X_0\left(\frac{Kl}{m+Kl}\right)^2,$$

and for the nth extraction,

$$X_n = X_0\left(\frac{Kl}{m+Kl}\right)^n.$$

Thus X_n, the quantity remaining in the first solvent (water), diminishes as n increases, and as m and K are respectively greater and less. Complete extraction is impossible, because although $\left(\frac{Kl}{m+Kl}\right)^n$ can approach zero very closely, it can never become equal to it.

Examples will facilitate comprehension of this formula. Suppose the problem be to determine how often 1000 c.c. of an aqueous solution of benzoic acid must be extracted with 200 c.c. of ether to remove all the benzoic acid from the solution. In this instance $l = 1000$ c.c., and $m = 200$ c.c. By experiment K is found to have approximately the value $\frac{1}{80}$; that is, if the concentration of the benzoic acid in the ethereal solution be represented by 80, that in the aqueous solution is expressed by 1. On substituting these values for l, m, and K respectively, the formula becomes

$$\frac{X}{X_0} = \frac{Kl}{m+Kl} = \frac{1000\times\frac{1}{80}}{200+1000\times\frac{1}{80}} = \frac{1}{17},$$

so that a single extraction with 200 c.c. of ether leaves $\frac{1}{17}$ of the benzoic acid in the aqueous solution. After three extractions with 200 c.c. of ether, there remains only $\left(\frac{1}{17}\right)^3 = \frac{1}{4913}$ of the acid, so that the extraction of the acid is practically complete.

For succinic acid $K=6$. A single extraction of 1000 c.c. of an aqueous solution of this acid with 200 c.c. of ether leaves $\frac{6000}{200+6000}=\frac{30}{31}$ of the acid still dissolved in the water. Repeated extraction is necessary to remove all the succinic acid from the aqueous solution.

Several agitations with small proportions of the solvent effect a more complete separation than that attained by employing the whole quantity for a single operation. An example will make this fact clear.

An aqueous solution of a substance is extracted with benzene, the coefficient of distribution being $\frac{1}{2}$. When one litre of the solution is agitated with a like volume of benzene in one operation, the proportion remaining in the water of the original quantity of material dissolved is $\frac{\frac{1}{2}}{1+\frac{1}{2}}=\frac{1}{3}$. On carrying out the extraction in two stages, half a litre of benzene being employed for each, the proportion of substance remaining dissolved in the water after the first agitation is $\frac{\frac{1}{2}}{\frac{1}{2}+\frac{1}{2}}=\frac{1}{2}$, and after the second $\frac{1}{2}\times\frac{1}{2}=\frac{1}{4}$. Since the same volume of benzene was employed in both instances, it follows that extraction in two stages gives a better separation than a single extraction. By employing the differential calculus, it can be proved to be best theoretically to extract an infinite number of times with infinitely small proportions of benzene.

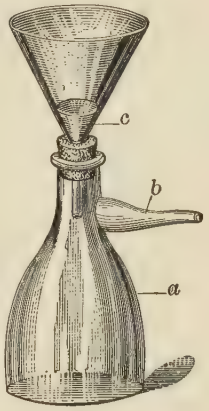


FIG. 19.—FILTERING-FLASK.

Separation of Solids and Liquids.—The separation of solids from liquids is effected by filtration, a process accelerated materially by attaching the funnel with a rubber stopper to a flask *a* (Fig. 19), connected through *b* to a water air-pump. To prevent rupture of the filter-paper, it must be supported by a hollow platinum cone *c* or by a perforated disk of porcelain.

24. *Separation of Solids from one Another.*—The processes for the separation of solids depend on difference in solubility. For a soluble and an insoluble substance the operation is very simple. If both substances be soluble, the method of *fractional crystallization* must be employed. The mixture is dissolved in the minimum quantity of a boiling liquid; on cooling the solution the less soluble substance crystallizes first. The mother-liquor is poured off as crystals of the second body begin to separate, and the second compound is crystallized either by further cooling or by concentrating the liquid by evaporation. Several repetitions of these processes are essential to the separation. Even with pure compounds

of very different solubilities, the method is not free from difficulty, because the solubility of one substance may be modified very considerably by the presence of another. Water, alcohol, ether, glacial acetic acid, benzene, and other substances are employed as solvents.

25. The foregoing account indicates solid substances to be purified usually by crystallization, and liquids by distillation. It is an indication of purity for the physical constants to remain unchanged after the substance has been submitted anew to the purification process. Although any physical constant could serve this purpose, the *melting-point* and the *boiling-point* are those most employed, because they are determined easily, and slight impurities exercise a very material influence upon them. Often they afford also a means of identifying substances. If a compound obtained by some process be thought to be one already known, it is strong evidence in favour of the supposition for the melting-point and the boiling-point of the substance to coincide with those of the compound supposed to be identical with it. For this reason determinations of melting-points and boiling-points are made very often.

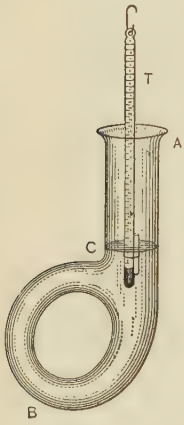


FIG. 20.—THIELE'S MELTING-POINT APPARATUS.

The best method of ascertaining whether two substances are identical is to mix them in approximately equal proportions and determine the melting-point of the mixture. When identity exists, the melting-point of the mixture will coincide with that of the two individual substances; when it does not, the mixture melts at a much lower and less sharply defined temperature.

THIELE has devised a very convenient apparatus for determining *melting-points* (Fig. 20). A small quantity of the substance is placed in a thin-walled capillary tube sealed at one end. This tube is attached to a thermometer *T* with its bulb dipping into a liquid of high boiling-point, such as concentrated sulphuric acid, olive oil, or liquid paraffin (31), the viscosity causing the tube to adhere to the thermometer. The liquid is contained in the apparatus *ABC*. Heating with a small flame at *B* induces circulation of the liquid, ensuring uniform warming of the thermometer and capillary tube. When the substance fuses, the thermometer is read.

The *boiling-point* is determined by heating the liquid to its boiling-point in a fractionation-flask with a high side-tube. To ensure the mercury column being surrounded completely by the vapour of the boil-

ing liquid short thermometers are employed. To avoid inconveniently small graduations, these thermometers are constructed to indicate a comparatively small range of temperature only, six or seven different instruments being employed for temperatures between −30° and 360°. They are designated "abbreviated" thermometers.

26. Sometimes physical constants other than the melting-points and boiling-points are employed in the investigation of organic compounds.

1. The *density* can be determined with the *pyknometer*, its most useful form being shown in Fig. 21. It consists of two thick-walled capillaries *a* and *b*, terminating in a wider tube *c*. The parts *a* and *b* are furnished with a millimètre-scale. The capacity of the apparatus is determined first, as well as that of the space between two divisions, by filling it several times to different divisions with water of known temperature, and then weighing. The liquid under investigation is then placed in the apparatus, and the pyknometer with its contents is weighed after the positions of the menisci in the capillaries have been observed; from the *data* thus obtained the density can be calculated.

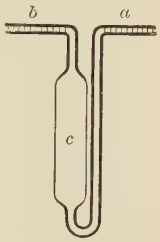


FIG. 21.—PYKNOMETER.

The coefficient of expansion of organic liquids is almost always much greater than that of water at the ordinary temperature, and the densities of these substances are influenced greatly by change of temperature. As a rule, there is an alteration of one unit in the third decimal place for each degree of temperature alteration.

As indicated by MENDELÉEFF, the density of such liquids at different temperatures can be expressed very approximately by the formula

$$D_t = D_0(1 - Kt),$$

D_0 being the density at 0°, D_t that at $t°$, and K a constant dependent on the nature of the liquid.

The number derived by division of the molecular weight by the density is termed the *molecular volume*.

2. The rotation of the *plane of polarization* is another constant of importance. Some substances, such as turpentine, a solution of sugar, and other materials, have the property of *rotating* out of its original position the plane of a ray of polarized light passing through them. This phenomenon is termed the *rotation of the plane of polarization*, and substances possessing this property are said to be *optically active*. *Polarimeters* have been constructed for measuring the angle through which the plane of polarization is rotated by an optically active substance, LAURENT'S form (Fig. 22) being one of the best known types. The yellow sodium-light of the burner *TT* is polarized in the part of the apparatus marked *BD*, and

then passes through a tube of known length (200–500 mm.) placed in the channel *L*. This tube contains the liquid or solution under examination. The part *OC* of the apparatus serves to measure the rotation of the plane of polarization.

The extent of the rotation of the plane of polarization is proportional to the length of the tube, and is expressed in various forms. One method is to state the rotation of a substance in terms of the effect produced by a given length of the tube described. The angle of rotation is read directly from the instrument, and usually is denoted by α. By convention, the *specific rotary power* is defined as the quotient obtained by dividing α by

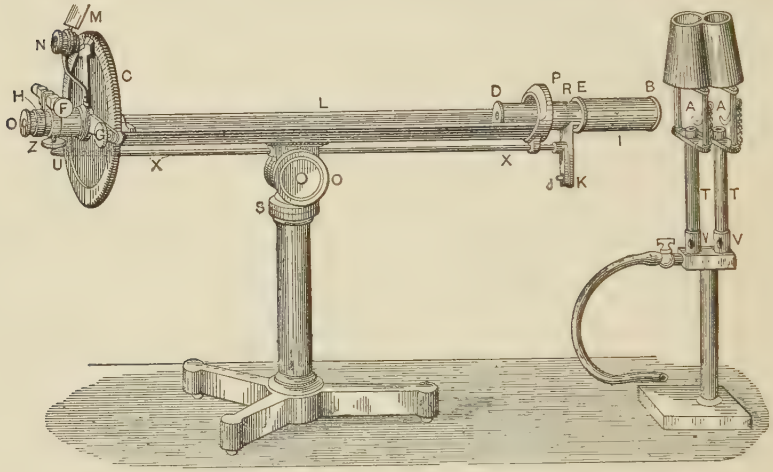


FIG. 22.—LAURENT'S POLARIMETER.

the product of the length of the tube into the density of the liquid This value is denoted by $[\alpha]$, so that

$$[\alpha]=\frac{\alpha}{ld},$$

l being the length of the tube, and d the density of the liquid. Under these conditions, $[\alpha]$ expresses the rotatory power of a substance per unit length of the tube (1 decimètre), and for unit weight of the substance divided into the unit of volume.

The extent of the rotation is dependent on the colour of the light, on the temperature, and for solutions on the nature of the solvent. The measurement is made often with sodium-light, which gives a yellow line in the spectroscope, denoted by *D*. With this type of light the symbol $[\alpha]_D$ is employed.

When the rotatory power of a substance is small, or when its slight solubility restricts its use to dilute solutions, the rotation often can be increased by adding a solution of boric acid, of molybdic acid, of uranium

salts, or of other substances. These bodies combine with the organic products to form compounds of much higher rotatory power.

The determination of the *refractive power* or *refraction* of liquid compounds is of great importance in organic research. A description of the apparatus employed is given in text-books of physics. The *index of refraction, n,* depends on the colour of the light employed, and generally is determined for the three principal lines of the hydrogen spectrum, for the yellow sodium line, or for five of the more brilliant lines of the helium spectrum. The difference in refraction for the various colours is termed *dispersion,* and also finds application in organic investigation.

The refraction also depends on the temperature, and therefore on the density of the liquid. On theoretical grounds, Lorentz, of Leyden, and Lorenz, of Copenhagen, consider the expression

$$\frac{n^2-1}{n^2+2}\cdot\frac{1}{d}$$

to be independent of the temperature, d representing the density. Within narrow limits of temperature, their view is supported by numerous experimental determinations. An empirical formula suggested by Eykman, $\frac{n^2-1}{n+0{\cdot}4}\cdot\frac{1}{d}$, remains constant over a range of temperature of more than 100°, and furnishes a much better expression of the independence of temperature. The product of these expressions by the molecular weight M,

$$\mathfrak{M}=\underset{\text{Lorentz's formula}}{\frac{n^2-1}{n^2+2}\cdot\frac{M}{d}} \quad \text{or} \quad \underset{\text{Eykman's formula}}{=\frac{n^2-1}{n+0{\cdot}4}\cdot\frac{M}{d}},$$

is named the *molecular refraction.* Reference will be made subsequently to the great importance of this constant.

The *molecular electric conductivity* is considered in 87, and the *absorption for ultraviolet light* in 337.

CLASSIFICATION OF ORGANIC COMPOUNDS.

27. The organic compounds are classed usually in two main divisions. One of these sections includes the *fatty* or *aliphatic compounds* (ἄλειφαρ, fat), and the other the *cyclic* or *ring compounds.* The first class owes its name to the inclusion in it of the animal and vegetable fats. Its members are called also *hormathic* compounds, their carbon atoms being arranged in a chain or row. The name of the second class is derived from the presence in its compounds of a closed chain or ring of atoms.

The aliphatic compounds can be regarded as derived from methane, CH_4. The most important cyclic derivatives are the *aromatic* compounds, so-called because many of them are characterized by an agreeable smell or aroma.

The important differences between the general properties of these two classes of compounds will be made evident in the sequel.

FIRST PART.

THE ALIPHATIC COMPOUNDS.

ALKANES, C_nH_{2n+2}.

28. The aliphatic compounds are defined in 27 as those derived from *methane*, CH_4. This generic relationship makes it desirable to begin the study of these compounds with this hydrocarbon.

Methane is a constituent of the gases evolved from volcanoes. It is liberated in coal-mines during the working of the coal-seams, and its mixture with air is named *fire-damp* by the miners. It is termed *marsh-gas* also, being present in the gases evolved from marshes by the decay of vegetable matter. It is an important constituent of coal-gas, being present in it to the extent of between 30 and 40 per cent.

It can be obtained by the following methods.

1. By SABATIER and SENDERENS's synthesis. When a mixture of hydrogen and carbon monoxide is passed over reduced nickel at temperatures between 250° and 300°, methane is formed:

$$CO+3H_2=CH_4+H_2O.$$

The nickel undergoes no apparent change, and can be utilized repeatedly. At temperatures between 230° and 300°, carbon dioxide reacts similarly with hydrogen in presence of finely-divided nickel:

$$CO_2+4H_2=CH_4+2H_2O.$$

2. Methane also can be synthesized directly from its elements by passing hydrogen through a heated tube containing reduced nickel mixed with very finely-divided carbon obtained by the previous decomposition of methane. An equilibrium is attained, corresponding at 475° and one atmosphere with 51 per cent. of methane:

$$CH_4 \rightleftarrows C+2H_2.$$

The action of nickel in methods 1 and 2 is probably due to the intermediate formation of an unstable compound of the formula NiH_2.

Pring found that pure carbon and pure hydrogen also combine directly without a catalyst at temperatures above 1100°, the equilibrium at 1200° corresponding with about 0·35 per cent. of methane.

3. By the action of water on aluminium carbide:

$$C_3Al_4+12H_2O=3CH_4+4Al(OH)_3.$$

Other methods of preparation are referred to in 75 and 83.

Physical and Chemical Properties.—Methane is an odourless and colourless gas of density 0·559 (air = 1). Its critical pressure is 55 atmospheres, and its critical temperature −82°. It boils at −165°, and solidifies at −186°. It is only slightly soluble in water, but dissolves more readily in alcohol. It is decomposed into carbon and hydrogen by the sparks of an induction-coil, or by means of the electric arc. Oxidizers such as nitric acid and chromic acid do not attack it, or only very slightly, whilst concentrated sulphuric acid and strong alkalis have no action on it. It burns with an almost non-luminous flame. Its mixture with air or oxygen has a violently explosive character, the reaction being in accordance with the equation

$$CH_4+2O_2=CO_2+2H_2O.$$

This "fire-damp" is one of the causes of explosion in coal-mines. Chlorine and bromine react with methane, replacing its hydrogen atoms by halogen atoms, and forming a hydrogen halide:

$$CH_4+2Cl=CH_3Cl+HCl.$$

The replacement of one atom by another is termed *substitution.* If chlorine or bromine be present in excess, the final product is carbon tetrachloride, CCl_4, or carbon tetrabromide, CBr_4.

29. There exists a series of hydrocarbons having general chemical properties similar to those of methane. Examples of these compounds are *ethane* C_2H_6, *propane* C_3H_8, *butane* C_4H_{10}, *pentane* C_5H_{12}, *hexane* C_6H_{14}, etc., *pentatriacontane*, $C_{35}H_{72}$, and *hexacontane* $C_{60}H_{122}$. These formulæ are special cases of the general expression C_nH_{2n+2}, for methane n being 1. The hydrocarbons C_nH_{2n+2} resemble methane in their power of resisting oxidation, and are unaffected by concentrated sulphuric acid, whilst halogens act on them with substitution of hydrogen and formation of compounds of the formulæ $C_nH_{2n+1}Cl$, $C_nH_{2n}Cl_2$, and so on.

The higher hydrocarbons can be obtained from those lower in the series by a process of building, exemplified by the formation of ethane from methane through replacement of a hydrogen atom by halogen,

and the subsequent action of sodium or calcium on the halide thus obtained:

$$2CH_3I+Na_2=C_2H_6+2NaI.$$

Propane can be prepared in accordance with the following equation:

$$CH_3I+C_2H_5I+Na_2=C_3H_8+2NaI.$$

In general, the hydrocarbon C_nH_{2n+2} is formed by the action of sodium on a mixture of the hydrocarbons $C_mH_{2m+1}I$ and $C_pH_{2p+1}I$, when $m+p=n$.

In addition to propane, butane, C_4H_{10}, is produced from $2C_2H_5I$, and ethane, C_2H_6, from $2CH_3I$, three hydrocarbons being obtained. A mixture of products is formed always in syntheses of this type.

Since methane can be prepared synthetically, obviously it is possible to synthesize each hydrocarbon of the formula C_nH_{2n+2}.

30. *Nomenclature.*—The hydrocarbons C_nH_{2n+2} are distinguished always by the termination "ane." The first four members, methane, ethane, propane, and butane, have special names; the others are denoted by the Greek or Latin numeral corresponding with the number of carbon atom, C_8H_{18} being termed *octane*, $C_{12}H_{26}$ *dodecane*, $C_{31}H_{64}$ *hentriacontane*, and so on.

It will be necessary often to consider groups of atoms unobtainable in the free state, but theoretically derivable by removal of a hydrogen atom from the hydrocarbons C_nH_{2n+2}. These groups have the general formula C_nH_{2n+1}, and are named *alkyl-groups*. They are denoted individually by changing the termination "ane" of the corresponding hydrocarbon into "yl," CH_3 being termed *methyl*, C_2H_5 *ethyl*, C_3H_7 *propyl*, C_4H_9 *butyl*, $C_{12}H_{25}$ *dodecyl*, etc.

The hydrocarbons C_nH_{2n+2} have the general name *alkanes*. They belong to the class of *saturated hydrocarbons*, because being saturated with hydrogen they are unable to take more hydrogen atoms into the molecule. They are also termed *paraffins* because paraffin-wax consists of a mixture of the higher members.

31. *Occurrence in Nature.*—The hydrocarbons C_nH_{2n+2} exist in nature in enormous quantities. Crude American petroleum consists of a mixture of a great number of these compounds, ranging from the lowest to the highest members of the series. From this petroleum, after treatment with acids and alkalis to free it from substances other than hydrocarbons of the formula C_nH_{2n+2}, three principal products are obtained by fractional distillation. The most volatile portion is named *petrol, gasoline, light petroleum, petroleum-ether, benzine, naphtha*, or

ligroïn. It distils between 40° and 150°, and contains lower members, chiefly C_6H_{14}, C_7H_{16}, and C_8H_{18}. It is employed extensively as motor-spirit, as a solvent for fats, oils, and resins, and in the removal of stains from clothing in the "Dry-cleaning process."

The steadily increasing demand for these products, especially for petrol, has led to the introduction of the "Cracking process." The less volatile constituents of the petroleum accumulate in great quantities and have a relatively small value. In this process they are distilled at about 500° and at a pressure of approximately twelve atmospheres, the large molecules of the higher hydrocarbons being decomposed into smaller molecules with the formation of a light oil. Owing to the relatively low percentage of hydrogen present in the less volatile constituents or *heavy oil* as compared with the more volatile constituents or *light oil*, cracking not only produces unsaturated hydrocarbons but leaves as a residue in the retorts a large proportion of carbon in the form of coke, and therefore gives a poor yield of light oil. Bergius cracks the petroleum constituents in an atmosphere of hydrogen at about 400° and 100 atmospheres, and thus almost completely obviates carbonization.

The method of Bergius is also applicable to the hydrogenation of finely powdered coal suspended in mineral oil. Should it prove to be practicable on the large scale, its technical importance would become very great, for the world's supply of coal is much greater than that of petroleum.

The portion distilling between 150° and 300° is ordinary *petroleum*, and is utilized on a large scale for lighting and cooking.

Further distillation above 300° yields *lubricating oil*, and then wax-like products, the residue in the still ultimately carbonizing. The residual product from the evaporation of American petroleum in the air is termed "Vaseline" or *petroleum-jelly*. It is semi-solid at the ordinary temperature, white when pure, and finds application in pharmacy as a substitute for fats in the preparation of ointments. It is employed as a lubricant for machinery, and also for covering the surfaces of metallic articles to hinder oxidation. As a protective coating it is superior to vegetable and animal fats, as in course of time they become rancid and attack the surface of the metal. Vaseline is free from acid, and remains unchanged on exposure to air.

Paraffin-wax is a mixture of the highest members of the series C_nH_{2n+2}, among them the hydrocarbons $C_{22}H_{46}$, $C_{24}H_{50}$, $C_{26}H_{54}$, and $C_{28}H_{58}$.

Some kinds of crude petroleum, notably that obtained from Java, contain a considerable proportion of these highest members. They are present in only relatively small amount in American petroleum. *Liquid paraffin* is a product of high boiling-point, obtained in the dry distillation of brown coal. *Earth-wax* or *ozokerite* occurs in Galicia,

and consists chiefly of paraffin-wax. This substance is obtained also in the dry distillation of the brown coal found in Saxony.

Asphalt (from ἄσφαλτος, unalterable) is a mixture of hydrocarbons of high molecular weight, and contains also compounds of oxygen, nitrogen, and sulphur in small proportions. It is present in large quantity in the celebrated "Pitch lake" of Trinidad, and in a similar lake in Venezuela, and is found also in Cuba. Artificial asphalt consists partly of oxidation-products of mineral-oil constituents of high boiling-point, analogous to the brown product formed by the action of atmospheric oxygen on paraffin-wax heated at a high temperature for a long time. It contains also residual pitch from the distillation of coal-tar.

32. The petroleum stored at depths up to 600 mètres in widely separated parts of the earth's interior is characterized by notable differences in composition. Probably the saturated hydrocarbons in it have been formed from fats under the influence of high temperature and great pressure. In confirmation of this hypothesis, ENGLER has prepared by distillation of train-oil under pressure a liquid very similar to natural petroleum. A mixture resembling petroleum and composed of saturated hydrocarbons is formed also by distilling *in vacuo* the salts of the higher fatty acids.

Many diverse suggestions have been made as to the origin of the enormous quantities of fats assumed to constitute the basis of petroleum. The best explanation is that of POTONIÉ, who regards the oil as having originated in the *sapropelium* or "putrefying ooze," a material rich in fats. Shallow fresh-water pools contain floating flora and fauna (*plankton*) of very minute dimensions (*microplankton*). They propagate rapidly, but the life of the individual is short. In consequence, a continuous shower of dead microplankton descends to the bottom of the pool, and subsequently decomposes to form *sapropelium*.

Caucasian petroleum consists mainly of naphthenes. PICTET has demonstrated the probability of its generation through the decomposition or resins, and therefore of its vegetable origin.

Homologous Series.

33. The general formula indicates each of the hydrocarbons C_nH_{2n+2} to differ in composition from the rest by $n \times CH_2$. The unimportance of the influence exerted by this difference on their chemical properties is mentioned in **29**.

Whenever organic compounds show great resemblance in their chemical properties, and have at the same time a difference in composition of $n \times CH_2$, they are said to be *homologous* (ὁμόλογος, corresponding), the name *homologous series* being given to such a group of compounds. As will be seen later, many such series are known.

Obviously this grouping simplifies the study of organic chemistry. Instead of having to consider the chemical properties of each com-

pound individually, it is sufficient to examine one member of a homologous series, as this procedure gives the principal characteristics of all the other members. In addition to the main properties common to the members of a homologous series, each individual member has its special characteristics. Except in a few instances, this book will not deal with them, because they need to be considered only in a more extensive survey of the subject.

The *physical properties*, such as the melting-points, boiling-points, densities, and solubilities, of the members of a homologous series, generally change uniformly as the number of carbon atoms increases. Usually the melting-points and boiling-points rise from the lower to the higher members of a homologous series.

A table of some of the physical constants of a number of normal (36) members of the paraffin series is given below. An inspection of this table reveals the first four members to be gases at the ordinary temperature, those from C_5 to C_{16} liquids, and the higher members solids. Although methane is odourless, the liquid members have a characteristic petroleum-like smell, a contrast to the odourless solid members. All are nearly insoluble in water.

The differences between the melting-points and boiling-points respectively of successive members of the series become smaller with increase in the number of carbon atoms, a phenomenon usual with homologous series.

Formula.	Name.	Melting-point.	Observed Boiling-point.	Calculated Boiling-point.	Density.
CH_4	Methane	−186°	−160°	−166·3°	0·415 (at −160°)
C_2H_6	Ethane	−172·1°	− 93°	− 95·3°	0·446 (at 0°)
C_3H_8	Propane	——	− 45°	− 43·1°	0·536 (at 0°)
C_4H_{10}	Butane	−135°	− 0·1°	− 0·4°	0·600 (at 0°)
C_5H_{12}	Pentane	−130·8°	36·3°	36·4°	0·627 (at 14°)
C_6H_{14}	Hexane	− 94·03°	68·9°	68·9°	0·658 (at 20°)
C_7H_{16}	Heptane	− 94·5°	98·4°	98·3°	0·683 ”
C_8H_{18}	Octane	− 57·4°	125·6°	125·1°	0·702 ”
C_9H_{20}	Nonane	− 51°	149·5°	149·8°	0·718 ”
$C_{10}H_{22}$	Decane	− 31°	173°	172·8°	0·730 ”
$C_{11}H_{24}$	Undecane	− 26°	194°	194·3°	0·774 at melting-point
$C_{12}H_{26}$	Dodecane	− 12°	214·5°	214·6°	0·773 ”
$C_{14}H_{30}$	Tetradecane	4°	252·5°	252·0°	0·775 ”
$C_{16}H_{34}$	Hexadecane	18°	287·5°	285·9°	0·775 ”
$C_{20}H_{42}$	Eicosane	36·5°	205°*	—	0·7775 ”
$C_{21}H_{44}$	Heneicosane	40·1°	215°	—	0·7778 ”
$C_{23}H_{48}$	Tricosane	47·4°	234°	—	0·7799 ”
$C_{31}H_{64}$	Hentriacontane	68·4°	302°	—	0·7799 ”
$C_{35}H_{72}$	Pentatriacontane	74°	331°	—	0·7813 ”
$C_{60}H_{122}$	Hexacontane	101°	—	—	—

* At 15 mm. pressure, and the same for those following.

For the boiling-points these differences are functions of the absolute temperature. SYDNEY YOUNG has induced the empirical formula

$$\Delta = \frac{144 \cdot 86}{T^{0 \cdot 0148\sqrt{T}}},$$

giving the difference in boiling-point of two successive members of the series, when T is the boiling-point on the absolute scale of the more volatile of the two homologues. The boiling-points in the fifth column of the table in this section were calculated by the aid of this formula.

The expression holds not only for this homologous series of hydrocarbons, but also for many other homologous series. The differences between the calculated and observed boiling-points are greatest for the lower members. For some homologous series the divergences are considerable, but can be proved usually to be due to association of the molecules of the compound in the liquid state, the molecular weight in this condition being twice, or a higher multiple of, that in the normal gaseous state.

YOUNG's formula holds for normal pressure, 760 mm. Often for the absolute boiling-points of two substances a and b the simple relation

$$\frac{T_a}{T_b} = \frac{T'_a}{T'_b}$$

obtains, T and T' being the absolute boiling-points of the substances at the same arbitrary pressure. Otherwise expressed, this equation means that the ratio of the boiling-points at different pressures often is constant.

EYKMAN has determined with great care the molecular refractions of the members of this series and of many other homologous series. His experiments have proved the difference between successive values not to be constant for the initial members of such series, but to become constant for the third or fourth member and those succeeding. This difference may be regarded as the refraction of the CH_2-group. Employing EYKMAN's formula (26), the difference for the α-line of the hydrogen spectrum is 10·260, and for the β-line 10·431.

Molecular refraction is mainly an additive property of the molecules. Despite the slight degree of its constitutive influence, deviations from pure addivity often furnish valuable indications of structural arrangement, as will be indicated frequently in the sequel.

Isomerism and Structure.

34. The only known substance with the formula CH_4 is methane. Similarly, there is only one compound having the formula C_2H_6, and one with the formula C_3H_8. There are known, however, two compounds with the formula C_4H_{10}, three with the formula C_5H_{12}, five with the formula C_6H_{14}, and so on. The phenomenon of two or more

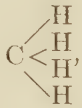
compounds being represented by one formula is termed *isomerism* (2), and compounds having the same formula are designated *isomerides*. Isomerism is explained by a consideration of the grouping of the atoms in the molecule.

One of two hypotheses might be adopted. In the first place, the arrangement of the atoms might be regarded as altering continually, a molecule being represented as like a planetary system having a configuration changing from moment to moment. This hypothesis fails to explain the phenomenon of isomerism, for it is not apparent how the four carbon atoms and ten hydrogen atoms in butane could form two different substances if their arrangement were indeterminate. There are trillions of molecules present in even one cubic millimètre, and all the possible configurations of these fourteen atoms must therefore be supposed to exist at any instant.

Isomerism can be understood at once by assuming a definite and unchanging arrangement of the atoms in the molecule, because then the difference in the properties of isomeric compounds can be explained by a difference in the arrangement of equal numbers of the same atoms.

> A definite and unchanging arrangement of the atoms in a molecule does not involve their being immovable with respect to one another, for they might revolve round a point of equilibrium without alteration in their order of succession.

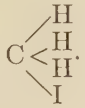
35. Since the phenomenon of isomerism leads to the assumption of a definite arrangement of the atoms in the molecule, it is necessary to solve the problem of how the atoms in the molecules of different compounds are grouped. The basis of the solution is the quadrivalency of the carbon atom. In methane the arrangement of the atoms can be represented by the formula



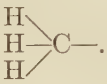
the four valencies of the carbon atom acting as four points of attraction, each holding a univalent hydrogen atom fast. No other arrangement is possible, because the hydrogen atoms cannot be bound to one another, the only point of attraction, or single bond, of each being already in union with one of the valencies of the carbon atom.

The arrangement of the atoms in ethane, C_2H_6, must now be investigated. This substance can be obtained by the action of sodium on methyl iodide, CH_3I (53), with a quadrivalent carbon atom, three

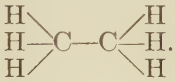
univalent hydrogen atoms, and one univalent iodine atom. It must therefore be represented thus:



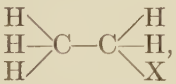
Sodium reacts with methyl iodide by withdrawing the iodine atoms from two molecules, with formation of ethane. The removal of the iodine atom sets free the carbon valency previously attached to this atom, with the production of two groups



Since the formula of ethane is C_2H_6, obviously the only arrangement of its atoms possible involves the union of the two free valencies of the methyl-groups:

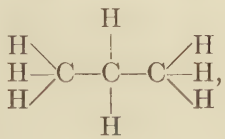


The arrangement of the atoms in propane can be determined in an exactly analogous manner. The formation of propane by the action of sodium on a mixture of methyl and ethyl halides is mentioned in **29**. Since ethane can be prepared by the interaction of sodium and methyl iodide, the formula of an ethyl halide can be only



X representing a halogen atom.

If the halogen be eliminated from this substance and from methyl iodide simultaneously, the residues unite, showing propane to have the structure



or shortly $H_3C \cdot CH_2 \cdot CH_3$.

Such an arrangement of symbols expressing the configuration of a molecule, and indicating the form or structure, is termed a *structural* or *constitutional formula.*

The following example makes clear the dependence of isomerism on differences in structure. One of the five known hexanes boils at 69°, and at 20·9° has the density 0·6583; another boils at 58°, and at 17·5° has the density 0·6701. The first is obtained by the action of sodium on *normal propyl iodide*, $CH_3 \cdot CH_2 \cdot CH_2I$. The argument respecting the constitution of normal propane indicates this hexane to have the structure

$$CH_3 \cdot CH_2 \cdot CH_2—CH_2 \cdot CH_2 \cdot CH_3.$$

On the assumption of its formation by the union of two propyl-groups it is named *dipropyl*.

In addition to this normal propyl iodide, an isomeride named *isopropyl iodide* is known. Both compounds can be converted readily into propane, $CH_3 \cdot CH_2 \cdot CH_3$. Assuming the isomerism to be due to a difference in the arrangement of the atoms in the molecule, the isomerism of the two compounds C_3H_7I can be explained only by a difference in the position occupied by the iodine atom in the molecule, because the arrangement of the atoms in propane is known, and each of the propyl iodides differs from propane only through the substitution of one hydrogen atom by iodine. If the constitution of normal propyl iodide be $CH_3 \cdot CH_2 \cdot CH_2I$, *iso*propyl iodide must have the structure

$$\begin{array}{c} H \\ \cdot \\ CH_3 \cdot C \cdot CH_3. \\ \cdot \\ I \end{array}$$

The hexane boiling at 58° is produced by the action of sodium on *iso*propyl iodide, and consequently must have the structure

$$\begin{array}{l} CH_3 \cdot CH \cdot CH_3 \\ \quad\quad | \\ CH_3 \cdot CH \cdot CH_3 \end{array} \quad \text{or} \quad \begin{array}{l} CH_3 \diagdown \\ \quad\quad CH \cdot CH \diagup CH_3 \\ CH_3 \diagup \quad\quad \diagdown CH_3 \end{array}.$$

Hence it is called *di*isopropyl.

Carbon Chains.

36. Evidently the facts cited make it reasonable to assume the existence of a bond between carbon atoms in the molecules of organic compounds. *This bond is very strong*, for the saturated hydrocarbons resist the action of powerful chemical reagents (**29**). The property possessed by carbon atoms of combining to form a series of many atoms, a *carbon chain*, like that in the hexanes described previously, constitutes a marked distinction between them and the atoms of all the other

elements. Such atoms either lack this power, or have it only in a very inferior degree. The enormous number of the carbon compounds is due to this property, in conjunction with the quadrivalency of the carbon atom.

A carbon chain like that in dipropyl is said to be *normal*, an example of a *branched* chain being furnished by di*iso*propyl. Each carbon atom in the normal chain is in direct union with not more than two others; in branched chains there are carbon atoms in direct union with three or four others. A normal-chain compound is denoted usually by putting *n* before its name; branched-chain compounds often are distinguished by the prefix *iso*.

A carbon atom united directly with only one other carbon atom is named *primary;* one united with two carbon atoms is termed *secondary;* one with three, *tertiary;* and one with four, *quaternary*. A carbon atom situated at the end of a chain is designated *terminal*. The carbon atoms of a chain are distinguished by numbers, the terminal one being denoted by 1, the one next it by 2, and so on; for example,

$$\underset{1}{CH_3}\cdot\underset{2}{CH_2}\cdot\underset{3}{CH_2}\cdot\underset{4}{CH_3}.$$

Sometimes the terminal atom is denoted by α, the one linked to it by β, and the succeeding one by γ, etc., but a terminal carbon atom in a CN-group, CHO-group, or COOH-group, is distinguished by ω, the next by α, and so on.

Law of the Even Number of Atoms.—The number of hydrogen atoms in the saturated hydrocarbons is even, their formula being C_nH_{2n+2}. All other organic compounds can be regarded as derived by exchange of these hydrogen atoms for other elements or groups of atoms, or by the removal of an even number of hydrogen atoms, or by both causes simultaneously. It follows that the sum of the atoms with uneven valency, such as hydrogen, the halogens, nitrogen, and phosphorus, must be always an even number. The molecule of a substance of the empirical composition $C_7H_2O_2N$ must be at least twice as great as this formula indicates, because $2H+1N$ is uneven.

Number of Possible Isomerides.

37. The quadrivalency of the carbon atom, coupled with the principle of the formation of chains of atoms, not only explains the existence of the known isomerides, but also renders possible the prediction of the existence of unknown compounds. Thus for a compound C_4H_{10} either the structure $CH_3\cdot CH_2\cdot CH_2\cdot CH_3$ or $\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!CH\cdot CH_3$ can be assumed.

and there are not any further possibilities. A pentane can have one of the structural formulæ

(1) $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3$; (2) $CH_3 \cdot CH_2 \cdot CH < \begin{matrix} CH_3 \\ CH_3 \end{matrix}$;

(3) $\begin{matrix} CH_3 \\ CH_3 \end{matrix} > C < \begin{matrix} CH_3 \\ CH_3 \end{matrix}$.

For a hexane one of the following five are possible:

(1) $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3$; (2) $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH < \begin{matrix} CH_3 \\ CH_3 \end{matrix}$;

(3) $CH_3 \cdot CH_2 \cdot \underset{\displaystyle CH_3}{\underset{|}{CH}} \cdot CH_2 \cdot CH_3$; (4) $CH_3 \cdot \underset{\displaystyle CH_3}{\underset{|}{CH}} \cdot \underset{\displaystyle CH_3}{\underset{|}{CH}} \cdot CH_3$;

(5) $CH_3 \cdot CH_2 \cdot C(CH_3)_3$.

If the principles given above be assumed, it will be impossible to find structural formulæ other than those mentioned.

Should it be possible to obtain the same number of isomerides as can be predicted thus, and no more, and should the products of synthesis or decomposition of any existing isomeride necessitate the assumption of the same structural formula as that required by the theory, these facts constitute a very important confirmation of the correctness of the principles underlying the theory. This correspondence of fact with theory has been proved to hold in many instances, and therefore affords an important means of determining the structure of a new compound, because if all the structural formulæ possible for the compound according to the theory be considered in turn, one of them will be found to be that of the substance.

Frequently the number of isomerides known is much smaller than that possible, because the number of possible isomerides increases very quickly with increase of the number of carbon atoms in the compound. Cayley has calculated that there are nine possible isomerides for C_7H_{16}, eighteen for C_8H_{18}, thirty-five for C_9H_{20}, seventy-five for $C_{10}H_{22}$, one hundred and fifty-nine for $C_{11}H_{24}$, three hundred and fifty-four for $C_{12}H_{26}$, eight hundred and two for $C_{13}H_{28}$, and so on. Chemists have not tried to prepare, for example, every one of the eight hundred and two possible isomerides of the formula $C_{13}H_{28}$, because their attention has been occupied by more important problems. There can, however, be no doubt as to the possibility of obtaining all these compounds, because the theoretical methods for synthesizing them are known. Although in theory the problem would present no difficulty, it might involve hindrances of an experimental nature.

Physical Properties of Isomeric Compounds.

38. Of the different isomerides the normal compound has the highest boiling-point.

The nearer a side-chain is to the terminal carbon atom, the lower is the boiling-point. Two side-chains attached to different carbon atoms produce a considerable reduction in the boiling-point. The isomeride with two side-chains in union with the penultimate carbon atom has the lowest boiling-point. The subjoined table affords confirmation of these statements.

Name.	Formula.	Boiling-point.
n-Octane	$CH_3 \cdot (CH_2)_6 \cdot CH_3$	125·5°
2-Methylheptane	$CH_3 \cdot CH(CH_3) \cdot (CH_2)_4 \cdot CH_3$	116·0°
3-Methylheptane	$CH_3 \cdot CH_2 \cdot CH(CH_3) \cdot (CH_2)_3 \cdot CH_3$	117·6°
4-Methylheptane	$CH_3 \cdot (CH_2)_2 \cdot CH(CH_3) \cdot (CH_2)_2 \cdot CH_3$	118·0°
2:5-Dimethylhexane	$CH_3 \cdot CH(CH_3) \cdot (CH_2)_2 \cdot CH(CH_3) \cdot CH_3$	108·3°
2:2′:3:3′-Tetramethylbutane	$CH_3 \cdot C(CH_3)_2 - C(CH_3)_2 \cdot CH_3$	104°

The isomeride with the most branched chain often has the highest melting-point.

In the examples cited the positions of the side-chains are denoted by figures, the carbon atoms of the main chain being numbered consecutively from one end to the other. This mode of notation is employed for all groups of organic compounds.

ALKANOLS OR ALCOHOLS, $C_nH_{2n+2}O$.

Methods of Formation and Constitution.

39. The *alkanols* or *alcohols* of the homologous series $C_nH_{2n+2}O$ can be obtained by the action of silver hydroxide on the alkyl halides:

$$C_nH_{2n+1}I + AgOH = C_nH_{2n+2}O + AgI.$$

It is usual to bring an alkyl iodide into contact with moist oxide of silver, the portion dissolved in the water reacting like silver hydroxide ("Inorganic Chemistry," **248**). The preparation of the alcohol from the iodide can be effected also by heating it with excess of water at 100°:

$$C_2H_5I + H_2O = C_2H_6O + HI.$$

When sodium reacts with an alcohol $C_nH_{2n+2}O$, one gramme-atom of hydrogen is liberated from each gramme-molecule of the alcohol, and a compound termed *sodium alkoxide* or *alcoholate*, $C_nH_{2n+1}NaO$, is produced. In presence of excess of water this product decomposes into sodium hydroxide and an alcohol. The sodium has replaced one atom of hydrogen, and neither it nor any other metal can replace more than one hydrogen atom, any excess of sodium added remaining unchanged. It follows that only one hydrogen atom in the alcohol molecule is replaceable by sodium.

When an alcohol reacts with trichloride or pentachloride of phosphorus, an alkyl chloride is formed:

$$3C_nH_{2n+2}O + PCl_3 = 3C_nH_{2n+1}Cl + H_3PO_3.$$

From these facts the constitution of the alcohols can be induced. Silver hydroxide can have only the structure Ag—O—H, its bivalent oxygen atom being united with its univalent silver and hydrogen atoms. The reaction following contact between silver hydroxide and an alkyl iodide must involve the severance of both the iodine atom from the alkyl-group and the silver atom from the hydroxyl-group. As a result,

the alkyl-group and the hydroxyl-group are afforded the opportunity of uniting through the liberated valency of each:

$$C_nH_{2n+1}\boxed{I+Ag}OH \rightarrow C_nH_{2n+1}—OH.$$

This method of formation proves the alcohols to contain a hydroxyl-group. Their preparation from alkyl iodides and water leads also to the same conclusion, and it receives further support from the two properties of alcohols mentioned on the preceding page. Evidently, if the structure of an alcohol be expressed by $C_nH_{2n+1}\cdot OH$, all the hydrogen atoms present except one are in direct union with carbon; and one hydrogen atom occupies a special position in the molecule, due to attachment to the oxygen atom with its second valency united with a carbon atom. It is reasonable to assume the special position occupied by this hydrogen atom to involve the special property of being the only hydrogen atom replaceable by alkali-metals. Moreover, sodium liberates hydrogen from another compound containing a hydroxyl-group. This compound is water, and for it the only constitution possible is H—O—H.

The fact of the alcohols being convertible into alkyl chlorides through the action of the chlorides of phosphorus is additional proof of the presence of a hydroxyl-group in the molecule. The empirical formulæ $C_nH_{2n+2}O$ and $C_nH_{2n+1}X$ show the halogen to have replaced OH. In this reaction the hydroxyl of the alcohol may be assumed to have changed places with the chlorine of the phosphorus compound:

$$3(C_nH_{2n+1}\cdot\overset{\curvearrowright}{OH})+\underset{\curvearrowleft}{Cl_3P}.$$

A consideration of the possible constitutional formulæ for substances having the general molecular formula $C_nH_{2n+2}O$ reveals the linkage of the oxygen atom to admit of only two possible formulæ, the compound C_2H_6O being either

$$\text{I. } CH_3\cdot CH_2\cdot OH, \quad \text{or} \quad \text{II. } CH_3\cdot O\cdot CH_3.$$

Since all the hydrogen atoms in the second formula have the same value, it cannot represent an alcohol, as it would not account for a very important property of these compounds, their interaction with the alkali-metals. The action of silver hydroxide on an alkyl iodide, or that of phosphorus chlorides on an alcohol, would accord equally ill with this formula, whereas formula I explains these reactions fully. It must therefore be adopted.

By this reasoning the constitutional formulæ of the alcohols have been induced from their properties. Inversely, *the constitutional formulæ represent all the chemical properties of the compounds,* being simply a short way of expressing them. The value of these formulæ is evident, the structural formula of a compound, established by the study of some of its properties, revealing the rest of these properties. The existence of properties thus deduced has been demonstrated in many instances by experiment.

Nomenclature and Isomerism.

40. The alkanols or alcohols of this homologous series are named after the corresponding hydrocarbons by changing the final *e* of the hydrocarbon name to *ol*; for example, *methanol, ethanol, propanol,* and so on. They were originally named after the alkyl-groups contained in them, the corresponding titles being *methyl alcohol, ethyl alcohol,* and *propyl alcohol.* In the table in this paragraph and in that in **41** the original

Name.	Formula.	Melting-point.	Boiling-point.	Density at 20° (d_4^{20}).
Alkanols, C_3H_8O				
1. Propanol-1 (Normal propyl)	$CH_3 \cdot CH_2 \cdot CH_2OH$	Vitreous	97°	0·804
2. Propanol-2 (*iso*Propyl)	$CH_3 \cdot CHOH \cdot CH_3$	−85·8°	82·4°	0·789
Alkanols, $C_4H_{10}O$				
1. Butanol-1 (Normal primary butyl)	$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2OH$	−79·6°	117°	0·810
2. Butanol-2 (Normal secondary butyl)	$CH_3 \cdot CH_2 \cdot CHOH \cdot CH_3$	Vitreous	100°	
3. Methyl-2-propanol-1 (*iso*Butyl)	$(CH_3)_2CH \cdot CH_2OH$	Vitreous	107°	0·806
4. Trimethylmethanol (Trimethylcarbinol *)	$(CH_3)_3C \cdot OH$	25·5°	83°	0·786
Alkanols, $C_5H_{12}O$				
1. Pentanol-1 (Normal primary amyl)	$CH_3 \cdot (CH_2)_3 \cdot CH_2OH$	—	138°	0·815
2. Methyl-3-butanol-1 (*iso*-Butylcarbinol)	$(CH_3)_2CH \cdot CH_2 \cdot CH_2OH$	−134°	131°	0·810
3. Methyl-2-butanol-1 (Secondary butylcarbinol)	$CH_3 \cdot CH(C_2H_5) \cdot CH_2OH$	—	128°	—
4. Pentanol-2 (Methylpropylcarbinol)	$CH_3 \cdot (CH_2)_2 \cdot CHOH \cdot CH_3$	—	119°	—
5. Methyl-3-butanol-2 (Methyl*iso*propylcarbinol)	$(CH_3)_2CH \cdot CHOH \cdot CH_3$	—	112·5°	—
6. Pentanol-3 (Diethylcarbinol)	$C_2H_5 \cdot CHOH \cdot C_2H_5$	—	117°	—
7. Methyl-3-butanol-3 (Dimethylethylcarbinol)	$(CH_3)_2C(OH) \cdot C_2H_5$	—	102°	—
8. Dimethyl-2:2-propanol-1 (Tertiary butylcarbinol)	$(CH_3)_3C \cdot CH_2OH$	—	112°	—

* *Carbinol* is an old name for methanol or methyl alcohol.

nomenclature is given in parentheses after the systematic names, the word "Alcohol" being omitted.

Isomerism may arise in three ways: by branching of the carbon chains; by changing the position of the hydroxyl-group; or through both these causes simultaneously. The three types are illustrated in the following table of the isomeric alcohols C_3 to C_5.

The table also indicates the hydroxyl-group in a *primary* alcohol to be joined to a primary carbon atom (36), and that in a *secondary* or a *tertiary* alcohol to a secondary or a tertiary carbon atom respectively. Similarly, any compounds capable of being regarded as produced by replacement of hydrogen in union with a primary, secondary, or tertiary atom are termed primary, secondary, or tertiary compounds. Primary alcohols are represented by the general formula $C_nH_{2n+1}—CH_2OH$,

secondary by $C_nH_{2n+1}—C(H)(OH)—C_mH_{2m+1}$,

and tertiary by $(C_nH_{2n+1})(C_mH_{2m+1})(C_pH_{2p+1})C—OH$.

General Properties of the Alkanols or Alcohols.

41. Some of the physical properties of the alcohols are given in this table, only normal primary compounds being included.

Name.	Formula.	Melting-point.	Boiling-point.	Difference of the Boiling-points.	Density, ($d_0°$).
Methanol (Methyl)	CH_3OH	− 97·1°	67·4°	13·3°	0·812
Ethanol (Ethyl)	C_2H_5OH	−114·15°	78°	18·5°	0·806
Propanol-1 (*n*-Propyl)	C_3H_7OH	−127°	96·5°	20·2°	0·817
Butanol-1 (*n*-Butyl)	C_4H_9OH	− 79·6°	116·7°	20·3°	0·823
Pentanol-1 (*n*-Amyl)	$C_5H_{11}OH$	—	137°	20°	0.829
Hexanol-1 (*n*-Hexyl)	$C_6H_{13}OH$	—	157°	18°	0·833
Heptanol-1 (*n*-Heptyl)	$C_7H_{15}OH$	− 36·5°	175°	19·5°	0·836
Octanol-1 (*n*-Octyl)	$C_8H_{17}OH$	− 17·9°	194·5°	18·5°	0·839
Nonanol-1 (*n*-Nonyl)	$C_9H_{19}OH$	− 5°	213°		0·842

This table, with that in 40, shows the normal compounds to have the highest boiling-points (38).

The augmentation of the molecule by addition of the CH_2-group is attended by an almost constant rise in boiling-point, although for the first members the rise is somewhat less than for the alcohols higher in the series. The association of the alcohol molecules renders Sydney Young's formula inapplicable (33).

The existence of this association is proved in many ways:

(1) The vapour-densities of the alcohols at temperatures slightly above their boiling-points are greater than indicated by their formulæ.

(2) The degree of association can be inferred from measurements of the capillarity and viscosity of the liquids.

(3) There subsists between the boiling-point and the molecular weight a relationship of the type

$$\frac{T}{\sqrt{M}}+1000\frac{\sqrt{M}}{T}=Const.,$$

T being the absolute boiling-point, and M the molecular weight. For many compounds the constant has the value 64, but it is much greater for associated substances, and increases with the degree of association.

(4) According to Trouton's rule

$$\frac{ML}{T}=21,$$

M being the molecular weight, L the latent heat of evaporation, and T the absolute boiling-point of a liquid. For water, the alcohols, and other associated liquids, the value of the quotient approximates to 26.

Various other formulæ are available for detecting association, an example being that of Jorissen,

$$n=\frac{193M^2}{T^2d},$$

n being the number of atoms in the molecule, M the molecular weight, T the boiling-point, and d the density at that temperature. For associated liquids T and d are abnormally high, and too low a value is obtained for n.

None of the formulæ gives an accurate measure of the degree of association.

The lower alcohols (C_1-C_4) are mobile liquids, the middle members (C_5-C_{11}) are of a more oily nature, whilst the higher members are solid at the ordinary temperature. In thin layers all are colourless. In thick layers they are slightly yellow, the colour becoming more marked with increase in the number of carbon atoms. The first members (C_1-C_3) are miscible in all proportions with water, but the solubility of the higher members diminishes quickly as the number of carbon atoms increases.

The smell of the lower members is spirituous, and that of the intermediate members disagreeable; whilst the solid members are odourless. Their density is less than 1.

Methanol or Methyl Alcohol, $CH_3\cdot OH$.

42. On the large scale *methyl alcohol* is obtained by the dry distillation of wood in iron retorts at as low a temperature as possible; and also by the better method of contact between wood and hot *producer-gas*, a mixture of carbon monoxide and nitrogen obtained by passing air over coke at a white heat. The mode of preparation originated the name *wood-spirit*. The products of the distillation are gases, an aqueous liquid, and wood-tar. The aqueous solution contains between

1 and 2 per cent. of methyl alcohol and a number of other substances, the chief being acetic acid (82) (*ca.* 10 per cent.) and acetone (111) (*ca.* 0·5 per cent.). The acetic acid is converted into calcium acetate by the action of lime, and the methyl alcohol is purified by fractional distillation, and by other methods.

A new method is the catalytic production on the industrial scale of methyl alcohol from carbon monoxide and hydrogen:

$$CO + 2H_2 = CH_4O.$$

Water-gas can be employed as a substitute for this gas mixture, because the proportion of the two gases can be varied within wide limits. This synthesis requires a pressure of two hundred atmospheres, and a temperature between 200° and 400° dependent on the catalyst employed. Besides methyl alcohol it produces also higher alcohols of this homologous series, the use of different catalysts affording a means of increasing or diminishing the yield of these higher alcohols. In the synthesis of methyl alcohol a mixture of zinc oxide and chromium oxide is employed as catalyst.

On the large scale methyl alcohol is utilized in the preparation of coal-tar dyestuffs and of formaldehyde, for the *denaturation* of spirit to render it unpotable (44), and for other operations.

Methyl alcohol burns with a pale-blue flame, and is miscible with water in all proportions, the mixing being accompanied by contraction and the development of heat. It is poisonous.

Ethanol or Ethyl Alcohol, $C_2H_5 \cdot OH$.

43. *Ethyl alcohol*, or ordinary alcohol, is produced artificially in enormous quantities. Its manufacture depends on a property possessed by *dextrose* (208), a sugar with the formula $C_6H_{12}O_6$, of decomposing in presence of *yeast-cells* into carbon dioxide and alcohol:

$$C_6H_{12}O_6 = 2C_2H_6O + 2CO_2.$$

On account of its cost, dextrose itself is not employed in the manufacture of alcohol, some substance rich in starch (225), $(C_6H_{10}O_5)_n$, such as potatoes, grain, or other material, being utilized as a substitute. By the action of *enzymes* (222), the starch is transformed almost completely into *maltose* (214), $C_{12}H_{22}O_{11}$, one molecule of this compound being then converted into two molecules of dextrose by the action of one molecule of water:

$$\underset{\text{Maltose}}{C_{12}H_{22}O_{11}} + H_2O = 2\underset{\text{Dextrose}}{C_6H_{12}O_6}.$$

The enzyme employed in the technical manufacture of maltose from starch is named *diastase*, and is present in malt. The reaction it induces is termed *saccharification*. When potatoes constitute the raw material, they are made first into a thin homogeneous pulp by

the action of steam under pressure between 140° and 150°, malt being added after cooling. At a temperature between 60° and 62°, the decomposition into maltose is completed within twenty minutes.

Yeast is then added to the maltose solution, and the fermentation is carried on between 23° and 25°. To separate the resulting alcohol from the other substances present, the product is submitted to distillation; and by employing a *fractionating-column* (Fig. 23), alcohol of 90 per cent. strength can be obtained, although the concentration of the alcohol in the fermented liquid does not exceed 18 per cent.

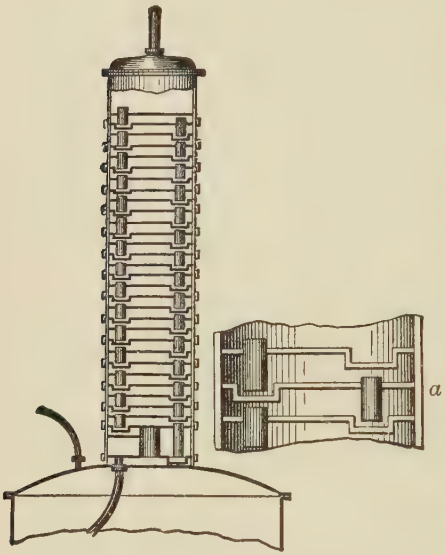


FIG. 23.—FRACTIONATING-COLUMN.

The thin liquid residue remaining in the still is termed *spent wash*, and is utilized for feeding cattle and for the manufacture of hydrogen cyanide (257). Amongst other products it contains almost all the proteins present in the raw material.

The crude spirit (*low wines*) so prepared is fractionated again carefully, alcohol of 96 per cent. by volume (*spirits*) being obtained. The fractions of higher boiling-point consist of an oily liquid of unpleasant odour, named *fusel-oil* (242), and containing chiefly amyl alcohols and other homologues. The residue is known as *spent lees*.

44. The alcohol of commerce ("spirits of wine") always contains water. To obtain anhydrous or *absolute* alcohol from it, lumps of quicklime are added to spirit containing a high percentage of alcohol until the quicklime shows above the surface of the liquid. The mixture is left for some days, or boiled for several hours under a reflux-condenser (17), and then is distilled. With this method the loss is relatively high. It is reduced to a minimum and the process is facilitated greatly by heating for some hours at 100° a spirit of high percentage with a small proportion of quicklime in an autoclave immersed in a water-bath. The spirit is then distilled. The preparation of absolute alcohol from dilute alcohol involves a preliminary concentration by distillation from a water-bath. The dehydration can be effected also by addition of solid potassium carbonate, the liquid separating into an

aqueous layer below and an alcoholic layer above. Alcohol of 91·5 per cent. by weight is obtained.

Absolute alcohol is a mobile colourless liquid of characteristic odour, and burns with a pale-blue non-luminous flame. Cooling with liquid air renders it very viscid, and ultimately causes crystallization. It is very hygroscopic, being miscible with water in all proportions with contraction and rise in temperature. The maximum contraction is obtained by mixing 52 volumes of alcohol with 48 volumes of water, the volume of the resulting mixture at 20° being 96·3 instead of 100.

The presence of water in alcohol can be detected by means of anhydrous cupric sulphate. When in contact with absolute alcohol, the salt remains perfectly colourless; if a trace of water be present, it develops a light-blue colour after several hours. The density, a physical constant often employed to ascertain the purity of liquid compounds, also can be utilized for the same purpose.

A simple and rapid process for the estimation of alcohol in aqueous mixtures is necessary for industrial and fiscal purposes, and a practical method, due to von Baumhauer, Mendeléeff, and others, consists in the determination of the density and temperature of such a mixture. A table has been prepared with great accuracy, showing the densities of mixtures of alcohol and water from 0 to 100 per cent., at temperatures between 0° and 30°. When the density and temperature of a given mixture have been determined, the percentage of alcohol can be found by reference to the table. In practice the density usually is determined with a delicate hydrometer.

In commerce and in the arts, the amount of alcohol is expressed normally on the Continent of Europe in *volume-percentage*, or the number of litres of absolute alcohol contained in 100 litres of the aqueous solution. In Great Britain the standard is *proof-spirit*. This name is derived from the old method of testing spirit by moistening gunpowder with it, and then bringing the mixture into contact with a lighted match. If the alcohol were "under proof," the powder did not take fire, but if there were sufficient alcohol present, the application of the light ignited the gunpowder, the spirit being then "over proof." When the proportion of alcohol and water was such as to make it just possible to set fire to the powder, the sample was described as "proof-spirit." Spirit weaker than proof-spirit is said to be *under proof*, that stronger than proof-spirit to be *over proof;* for example, a spirit 5° under proof would contain in each 100 volumes the same quantity of alcohol as 95 volumes of proof-spirit, and a spirit 5° over proof would need 5 volumes of water added to each 100 volumes to convert it into proof-spirit. By British Act of Parliament "proof-spirit" is defined as "such a spirit as shall at a temperature of 51° F. weigh exactly $\frac{12}{13}$ of an equal measure of distilled water," corresponding with a spirit containing 57·1 per cent. of alcohol by volume or 49·3 per cent. by weight.

For scientific purposes the proportion of alcohol is expressed usually in percentage by weight, or the number of grammes of alcohol contained in 100 grammes of the aqueous solution. These percentage-numbers are not identical, the percentages by weight being smaller than those by volume for a spirit of any given concentration.

The greater part of the alcohol produced is consumed as beverages, any detrimental physiological effects being augmented by the impurities, especially by fusel-oil.

Two classes of alcoholic beverages are recognized, distilled and undistilled liquors.

Distilled (about 50 per cent of alcohol).	Undistilled.
Brandy or *cognac*, from wine.	*Beer*, from fermented malt and hops (3 to 6 per cent. of alcohol).
Whisky, from fermented solution of malt.	*Wine*, fermented grape-juice (8 to 10 per cent. of alcohol).
Rum, from fermented solution of sugar.	"*Fortified*" *wines*, such as *port*, *sherry*, and *madeira*. They are wines with added alcohol. (Natural wine never contains more than about 10 per cent. of alcohol.)
Gin, like whisky, but flavoured with juniper.	

Alcohol is utilized in manufacture for the preparation of lacquers, varnishes, dyes, important pharmaceutical preparations such as chloroform, chloral, iodoform, and others, and as a motive power for motor-vehicles. It is employed also for the preservation of anatomical specimens. It is a good solvent for many organic compounds, and for this purpose finds wide application in laboratory-work.

Certain industrial operations require the use of absolute alcohol instead of the alcohol of 96 per cent. strength obtained by the ordinary mode of distillation. On the large scale aqueous alcohol can be rendered absolute by distilling a mixture of it with benzene, the method depending on a peculiar property of the system benzene—alcohol—water. These substances yield a ternary mixture with a minimum boiling-point 64·9°, this mixture containing 7·4 parts of water, 18·5 parts of alcohol, and 74·1 parts of benzene. The system alcohol—benzene has the minimum boiling-point 68·2°, the mixture consisting of 32·4 parts of alcohol and 67·6 parts of benzene. On distilling through a fractionating-column aqueous alcohol containing a sufficient proportion of benzene, the ternary mixture boiling at 64·9° passes over, this product distilling until all the water has been eliminated from the liquid. The binary mixture of boiling-point 68·2° then volatilizes, the ultimate residue in the still consisting of absolute alcohol. It is drawn off, and the recovered benzene is employed for a repetition of the process.

On account of the extensive application of alcohol to manufacturing processes, some industries would be paralysed if the necessary spirit were subject to the same excise-duty as alcohol intended for consumption. Accordingly in some countries the alcohol employed in manufacture is made unfit for drinking (*denatured* or *methylated*) by the addition of materials imparting to it a nauseous taste, and is sold duty-free. On the Continent of Europe crude wood-spirit is utilized for this purpose, and in Great Britain this adulterant is supplemented by the addition of a small proportion of naphtha and other substances. The sale of denatured alcohol is permitted also in the United States.

A test for ethyl alcohol is the formation of iodoform on the addition of iodine and potassium hydroxide (**146**).

Propanols or Propyl Alcohols, $C_3H_7 \cdot OH$.

45. Two *propyl alcohols* are known, one boiling at 97° and having the density 0·804, the other boiling at 82·4° and having the density 0·789. In accordance with the principles stated, only two isomerides are possible:

$$\underset{\text{Normal propyl alcohol}}{CH_3 \cdot CH_2 \cdot CH_2OH}, \quad \text{and} \quad \underset{\textit{iso}\text{Propyl alcohol}}{CH_3 \cdot CH(OH) \cdot CH_3}.$$

The structure to be assigned to the substance with the higher boiling-point and that to the substance with the lower can be determined by submitting the substances to oxidation. From each of these alcohols a compound with the formula C_3H_6O is obtained, but these oxidation-products are not identical. On further oxidation, the compound C_3H_6O (propionaldehyde), produced from the alcohol of higher boiling-point, yields an acid $C_3H_6O_2$, termed propionic acid; whereas the substance C_3H_6O (acetone), formed from the alcohol of lower boiling-point, is converted into carbon dioxide and acetic acid, $C_2H_4O_2$:

$$C_3H_8O \text{ (propanol-1, b.p. } 97°) \rightarrow C_3H_6O \text{ (propanal)} \rightarrow \rightarrow C_3H_6O_2 \text{ (propionic acid)};$$

$$C_3H_8O \text{ (propanol-2, b.p. } 82·4°) \rightarrow C_3H_6O \text{ (acetone)} \rightarrow \rightarrow CO_2 + C_2H_4O_2 \text{ (acetic acid)}.$$

Propionic acid has the constitution $CH_3 \cdot CH_2 \cdot COOH$, and acetone $CH_3 \cdot CO \cdot CH_3$, as will be proved subsequently. Only the normal alcohol is capable of forming propionic acid, the production of this substance being due to the replacement of two hydrogen atoms by one oxygen atom, and with the normal alcohol this exchange can yield only a compound with the structure assigned to propionic acid. On the other hand, the formation of a derivative with the constitution of acetone by removal of two hydrogen atoms from a compound C_3H_8O is possible only for a substance with the structure of *iso*propyl alcohol.

The alcohol of higher boiling-point must therefore be *n*-propyl alcohol, and that boiling at the lower temperature must be *iso*propyl alcohol.

Oxidation affords a general method for distinguishing primary alcohols from secondary alcohols. By referring to the formulæ given in 40, all primary alcohols are seen to contain the group $-CH_2OH$, convertible by oxidation into the carboxyl-group $-C\begin{matrix}=O\\ \diagdown OH\end{matrix}$, the characteristic group of organic acids. All secondary alcohols contain the group $H\cdot\overset{|}{\underset{|}{C}}\cdot OH$, and removal of the two hydrogen atoms from this complex yields the group $\overset{|}{\underset{|}{C}}{:}O$, characteristic of the *ketones* (110), the homologues of acetone. *The oxidation of a primary alcohol and that of a secondary alcohol produce respectively an acid and a ketone with the same number of carbon atoms as the original alcohol.*

A further induction may be made from these reactions. In the conversion of normal propyl alcohol into propionic acid, as well as of *iso*propyl alcohol into acetone, the oxidation occurs at the carbon atom already attached to oxygen. This rule is general, and can be stated as follows: *when an organic compound is submitted to oxidation, the molecule is attacked at the part already containing oxygen—that is, where oxidation has begun already.*

Normal propyl alcohol is obtained by fractionation of fusel-oil, and is a colourless liquid of agreeable odour. It is miscible with water in all proportions. *iso*Propyl alcohol is also a liquid, and is not present in fusel-oil, but can be prepared by the reduction of acetone (111 and 150).

Butanols or Butyl Alcohols, $C_4H_9\cdot OH$.

46. Four *butyl alcohols* are known (*cf.* Table, 40), the number possible according to theory, and it is necessary to consider whether the theoretically possible formulæ are in accord with the properties of the four isomerides. On oxidation, the two alcohols boiling at 117° and 107° respectively yield acids with the same number of carbon atoms. They must therefore have the structures 1 and 3 (*Ibid.*), since each contains the group $-CH_2OH$. For reasons mentioned subsequently, the alcohol boiling at 117° is considered to have the normal structure (1), and that boiling at 107° the structure (3). A third butyl alcohol, boiling at 100°, is converted by oxidation into a ketone with the same number of carbon atoms, proving it to be a secondary alcohol corresponding with structure (2). Lastly, for the fourth, a solid at the ordinary temperature, melting at 25·5° and boiling at 83°, there remains only the fourth structure, that of a tertiary

alcohol, three of the theoretically possible structural formulæ having been assigned to the other isomerides. This constitution, indicated by a process of elimination for the alcohol melting at 25·5°, accords with its chemical behaviour. On oxidation, for example, it yields neither an acid nor a ketone with four carbon atoms, but undergoes immediate decomposition into substances with a smaller number of carbon atoms in the molecule. Since to yield by oxidation an acid with the same number of carbon atoms in the molecule, an alcohol must contain the group $—CH_2OH$, and to produce a ketone with the same number of carbon atoms in the molecule, it must contain the group $H\cdot\overset{|}{\underset{|}{C}}\cdot OH$, obviously neither of these types can be obtained from a tertiary alcohol. If the oxidation follow the general rule, and occur at the carbon atom already in union with oxygen, it must cause the decomposition of the molecule.

The reasoning holds for tertiary alcohols in general, oxidation affording a means of distinguishing between primary, secondary, and tertiary alcohols. The experimental proof can be summed up as follows:

On oxidation a primary alcohol yields an acid with the same number of carbon atoms in the molecule; a secondary alcohol yields a ketone with the same number of carbon atoms in the molecule; but a tertiary alcohol undergoes immediate decomposition into compounds with a smaller number of carbon atoms in the molecule.

There are other methods available for distinguishing between primary, secondary, and tertiary alcohols, one of the simplest being based on the decomposition of the alcohols by heat. The primary compounds are stable up to the temperature of 360°, the boiling-point of mercury; but the secondary derivatives are decomposed. The secondary alcohols can withstand the temperature of 218°, the boiling-point of naphthalene, whilst the tertiary alcohols undergo decomposition. To decide whether a particular alcohol is primary, secondary, or tertiary, it is only necessary to determine its vapour-density by means of Victor Meyer's apparatus at the two temperatures cited, the normal or abnormal nature of the results at the two temperatures indicating the type of alcohol under investigation.

Normal butyl alcohol is manufactured now from starch and other carbohydrates by yeasting under the influence of *Bacillus amylobacter*.

Pentanols or Amyl Alcohols, $C_5H_{11}\cdot OH$.

47. The alcohols with five carbon atoms in the molecule are termed *amyl alcohols*. Eight isomerides are possible, and all are known (*cf.* Table, 40). They are liquids with a disagreeable odour like that of fusel-oil. *iso*-Butylcarbinol, $(CH_3)_2CH\cdot CH_2\cdot CH_2OH$, and secondary butylcarbinol, $CH_3\cdot CH(C_2H_5)\cdot CH_2OH$, are the principal constituents of that oil (43).

Secondary butylcarbinol furnishes a very remarkable example of

isomerism. In 34 the arrangement of the atoms in the molecule is proved to account for the phenomenon of isomerism. A careful study of the properties of a compound makes it feasible to assign to it a structural formula, to the exclusion of all the other formulæ possible for its known molecular composition. On the other hand, any given structural formula represents only *one* compound, such a formula being the expression of a very definite set of properties. The possession of dissimilar characteristics by two compounds must find expression in their structural formulæ.

Nevertheless, there are three isomeric amyl alcohols, proved by careful examination to have the same structural formula:

$$\begin{matrix} CH_3 \\ C_2H_5 \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} H \\ CH_2OH. \end{matrix}$$

This constitution is established through their conversion by oxidation into valeric acid with the structure

$$\begin{matrix} CH_3 \\ C_2H_5 \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} H \\ COOH, \end{matrix}$$

as can be proved readily by synthesis (**164**).

The three amyl alcohols with this constitution have identical chemical properties. Nearly all their physical constants are the same, but one of them serves to distinguish the substances from one another. When a beam of plane-polarized light is passed through layers of these alcohols, the plane of polarization is rotated by one isomeride to the left, and by another to the right, whilst the third alcohol does not produce any rotation. The first two are said to be *optically active* (**26**, 2).

Since the difference between optically active compounds depends only on a physical property, their chemical properties being identical, it may be asked whether this difference is not purely physical, and due to differences in the arrangement of the molecules such as are supposed to exist in dimorphous substances. The objection to this view is twofold.

First, differences in the arrangement of the molecules can be supposed to exist only with solids, because only their molecules have a fixed position relative to one another. The molecules of liquids and gases are assumed to be free to move; but they also afford examples of optical activity. For liquids there is still the possibility of freedom of movement being characteristic, not of the molecules themselves, but of conglomerations of them arranged in a definite manner. If this phenomenon were the cause of optical activity, on conversion into gases of normal vapour-density, optically active liquids should produce no rotation in the plane of polarization. Their power of producing such

rotation was demonstrated by Biot, and later by Gernez. The phenomenon cannot be attributed to a difference in the arrangement of the molecules, because in a vapour of normal density each molecule is capable of independent motion.

Second, the optical activity is displayed in derivatives of optically active substances.

Hence it follows that *an explanation of the rotation of the plane of polarization by liquids and dissolved substances must be sought in the internal structure of the molecules.*

48. Pasteur regarded optically active molecules as having an asymmetric structure, two configurations being possible. These forms are mirror-images, but cannot be superimposed, their relationship resembling that of a right-handed and a left-handed glove. One of the configurations must belong to the dextrorotatory isomeride, and the other to the lævorotatory modification.

van 't Hoff imparted a more concrete form to this conception by his discovery of the presence in most optically active compounds of at least one carbon atom united with four dissimilar atoms or groups. He designated such a carbon atom an *asymmetric carbon atom.*

When two of the groups attached to such an atom become similar, the asymmetry vanishes, and with it the optical activity of the compound. Consideration of an example will facilitate the comprehension of this phenomenon.

The *lævorotatory amyl alcohol*, with the constitution

$$\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}H\\CH_2OH,\end{matrix}$$

is converted by the action of gaseous hydrogen iodide into *amyl iodide*, with the structural formula

$$\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}H\\CH_2I.\end{matrix}$$

This compound is *optically active.* By means of nascent hydrogen the iodine atom is replaced by hydrogen, with formation of *pentane*,

$$\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}H\\CH_3.\end{matrix}$$

This compound is *optically inactive.*

If amyl iodide be subjected to the action of ethyl iodide in the presence of sodium, a *heptane*,

$$\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}H\\CH_2\cdot C_2H_5,\end{matrix}$$

is produced, and this substance is *optically active.*

An examination of these three optically active substances shows them to differ from optically inactive pentane in having four dissimilar groups attached to the central carbon atom, whereas in the inactive pentane two (methyl) are similar.

Pasteur's *molecular asymmetry* of carbon compounds with an asymmetric carbon atom is explained by the following considerations.

The quadrivalency of the carbon atom has its origin in four points of attraction situated on its outer surface, it being able to unite with atoms or groups of atoms in four directions. The only supposition about these directions in agreement with the facts postulates *the carbon atom to be at the centre of a regular four-sided figure (tetrahedron) with its valencies directed toward the angles* (Fig. 24). On putting the groups R, P, and Q of compounds CR_2Q_2, CR_2PQ or CR_3P in different positions in two atom models,* by rotating the models it is possible always to superimpose the like groups, showing the two forms to be identical. Such compounds do not exhibit optical isomerism.

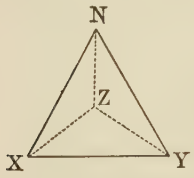


FIG. 24.—CARBON TETRAHEDRON.

For compounds C·RPQS, containing four different groups and therefore an asymmetric carbon atom, the possibility of the existence of two isomeric forms is indicated. It is seen from Figs. 25 and 26 (and still better from models) that for these four groups two arrangements which cannot be superimposed in any position are possible, although they resemble one another as an object resembles its reflection in a mirror. Such a figure has no plane of symmetry, hence the name "Asymmetric carbon atom."

These considerations explain why one isomeride causes as much dextrorotation as the other lævorotation, for the arrangement of the groups relative to the asymmetric carbon atom must be the cause of the rotation of the plane of polarization. If the arrangement of the groups in Fig. 25 produce dextrorotation, then the inverse arrangement in the isomeride in Fig. 26 must cause an equal rotation, but in the opposite direction.

As mentioned previously, with one asymmetric carbon atom in the molecule three, and not merely two, isomerides are possible, a dextrorotatory, a lævorotatory, and an optically inactive isomeride. The

* The comprehension of this subject will be facilitated considerably by the construction of several models of carbon atoms with their valencies. A sphere to represent the carbon atom is cut from a cork, the valencies being indicated by moderately thick wires about ten centimètres long, with ends filed to a point. These are fixed in the cork sphere in the manner shown in Fig. 24. To demonstrate the union of the atoms or groups of atoms, cork spheres of different colours are fastened to the ends of the wires, the different colours indicating dissimilar groups.

optically inactive substance has been proved to consist of equal parts of the dextrorotatory and of the lævorotatory compound. Since the rotations are equal in amount, but different in direction, their sum has no effect on the plane of polarization.

This isomerism in space is termed *stereochemical isomerism* or *stereoisomerism*. It is not indicated in the ordinary structural formulæ written in one plane, hence the apparent contradiction of a single structural formula representing two different compounds. The out-

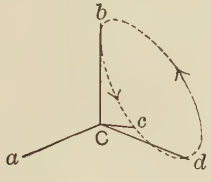


Fig. 25.

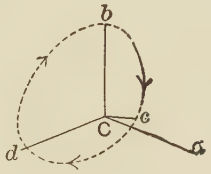


Fig. 26.

Asymmetric Carbon atoms.

line of van 't Hoff's theory given here shows it to support the fundamental principle of all isomerism having its origin in a difference in the arrangement of the atoms in the molecule.

The researches of Bragg on the structure of the diamond have furnished a striking confirmation of the accuracy of the foregoing deductions as to the directions of the valencies of the carbon atom. The diffraction phenomena exhibited by Röntgen rays on passage through crystals afford a means of determining the arrangement of the atoms in crystal molecules ("Inorganic Chemistry," 213). The method has proved the diamond to be constructed of regular tetrahedra, each having a carbon atom at its centre and a carbon atom at each of its four angles.

Higher Alkanols or Alcohols, $C_nH_{2n+1}\cdot OH$.

49. The properties of the *higher alcohols* are mentioned in 41. Here may be cited *cetyl alcohol*, $C_{16}H_{33}\cdot OH$, obtained from spermaceti, and *myricyl alcohol*, $C_{30}H_{61}\cdot OH$, produced from wax. The number of isomerides of these higher compounds possible is very great, whilst the number actually known is small. Of the higher members of the series, only the normal primary compounds are known.

Alkanolates or Alkoxides.

50. *Alkoxides* (alcoholates) are compounds obtained from alcohols by exchange of the hydroxyl-hydrogen atom for metals (39). The

most typical examples are *sodium methoxide* (methylate), $CH_3 \cdot ONa$, and *sodium ethoxide* (ethylate), $C_2H_5 \cdot ONa$. Each is a white powder, and each yields a crystalline compound with the corresponding alcohol. They dissolve readily in the alcohols, and, as will be seen later, are employed extensively in synthesis. Formerly the addition of water to a solution of an alkoxide was assumed to convert it completely into an alkali-metal hydroxide, liberating an equivalent quantity of alcohol; but Lobry de Bruyn demonstrated the partial truth of this assumption, and the attainment of an equilibrium in the reaction:

$$C_2H_5ONa + H_2O \rightleftarrows C_2H_5OH + NaOH.$$

A proof of this interpretation is given in 55. It follows that a solution of sodium hydroxide in alcohol is decomposed partially into water and sodium alkoxide.

The alcoholic solution of sodium ethoxide is obtained usually by dissolving pieces of sodium in absolute ethyl alcohol. In consequence of oxidation to aldehyde (106), it becomes brown gradually. On the other hand, the solution of sodium methoxide in methyl alcohol remains unaltered, and therefore finds wider application in synthesis than that of sodium ethoxide.

Only the alkali-metals react directly with alcohols to produce alkoxides. The corresponding derivatives of other metals can be prepared by the interaction of solutions in liquid ammonia of a potassium alkoxide and a salt, an example being the precipitation of barium ethoxide by the action of potassium ethoxide on barium nitrate:

$$2C_2H_5OK + Ba(NO_3)_2 = (C_2H_5O)_2Ba + 2KNO_3.$$

The alkoxides of calcium, strontium, and lead have been prepared similarly.

HALOGEN-ALKANES OR ALKYL HALIDES, ESTERS, AND ETHERS.

51. In inorganic chemistry many compounds containing a hydroxyl-group are known. They are termed bases, and display a close similarity in properties, attributable to their common possession of the hydroxyl-group present in their aqueous solutions as an ion.

An aqueous solution of alcohol does not conduct an electric current, the alcohol not being ionized. This view is supported by the fact that such a solution is not alkaline, and therefore lacks hydroxyl-ions. Nevertheless the alcohols possess a basic character, for they resemble bases in combining with acids with elimination of water:

$$\underset{\text{Alcohol}}{M\cdot\boxed{OH+H}}\cdot R=\underset{\text{Ester}}{M\cdot R}+HOH.$$

The substances formed are comparable with the salts of inorganic chemistry, and are termed *compound ethers* or *esters*. The difference between the nature of bases and that of alcohols is displayed in the mode of formation of salts, a process quite unlike that employed in the production of esters. A salt is formed from an acid and base instantaneously, the reaction being between the ions, because the hydrogen ion of the acid unites with the hydroxyl-ion of the base ("Inorganic Chemistry," **66**):

$$\underset{\text{Base}}{[\dot{B}+OH']}+\underset{\text{Acid}}{[\dot{H}+Z']}=\underset{\text{Salt}}{[\dot{B}+Z']}+H_2O.$$

In contrast with this process the formation of esters is very slow, especially at the ordinary temperature, the reaction being between the non-ionized alcohol and the acid:

$$\underset{\text{Alcohol}}{R\cdot OH}+\underset{\text{Acid}}{[\dot{H}+Z']}=\underset{\text{Ester}}{R\cdot Z}+H_2O.$$

Normally reactions between ions are instantaneous, those between molecules slow.

Many bases can lose water, with formation of anhydrides or oxides, and alcohols behave similarly. By the abstraction of one molecule of water from two molecules of an alcohol, compounds termed *ethers* with the general formula $C_nH_{2n+1}—O—C_nH_{2n+1}$ are formed. By elimi-

nation of water from two different alcohols, compounds named *mixed ethers* with the general formula

$$C_nH_{2n+1}—O—C_mH_{2m+1}$$

are produced.

Halogen-alkanes or Alkyl Halides.

52. The *alkyl halides* can be regarded as the hydrogen-halide esters of the alcohols, a view in accord with their formation from an alcohol and a hydrogen halide:

$$C_nH_{2n+1}\boxed{OH+H}X = C_nH_{2n+1}X + H_2O.$$

In preparing alkyl halides by this method, the alcohol is saturated first with the dry hydrogen halide, and heated then in a sealed tube or under a reflux-condenser. The reaction may be induced also by heating the alcohol with sulphuric acid and sodium or potassium halide:

$$C_2H_5OH + H_2SO_4 + KBr = C_2H_5Br + KHSO_4 + H_2O.$$

Another method of formation for alkyl halides is mentioned in **39.** It is considered more fully here.

Action of Phosphorus Halides on Alcohols.—Sometimes these substances react very energetically. In preparing alkyl bromides and iodides, it is usual to employ phosphorus with bromine or iodine instead of the bromide or iodide of phosphorus itself. For example, in the preparation of ethyl bromide, red phosphorus is added to strong alcohol, in which it is insoluble. Bromine is added then drop by drop, the temperature of the liquid being kept from rising by a cooling agent. Each drop of bromine unites with phosphorus to form phosphorus tribromide, and it reacts with the alcohol, producing ethyl bromide:

$$PBr_3 + 3C_2H_5OH = PO_3H_3 + 3C_2H_5Br.$$

The careful addition of bromine is continued until a quantity corresponding with that required by the equation has been introduced. The mixture is kept for a time, so as to render the reaction as complete as possible, the final product consisting chiefly of phosphorous acid and ethyl bromide. Since the ester boils at 38·4°, and the acid is not volatile, it is possible to separate them by distillation, effected by immersing the flask containing the mixture in a water-bath heated above the temperature mentioned.

53. The following table gives some of the physical properties of the alkyl halides:

Alkyl-group.	Name.	Chloride.		Bromide.		Iodide.	
		Boiling-point.	Density.	Boiling-point.	Density.	Boiling-point.	Density.
CH_3	Methyl	−23·7°	0·952(0°)	4·5°	1·732(0°)	45°	2·293(18°)
C_2H_5	Ethyl	12·2°	0·918(8°)	38·4°	1·468(13°)	72·3°	1·944(14°)
C_3H_7	*n*-Propyl	46·5°	0·912(0°)	71°	1·383(0°)	102·5°	1·786(0°)
C_4H_9	*n*-Prim. butyl	78°	0·907(0°)	101°	1·305(0°)	130°	1·643(0°)
C_5H_{11}	*n*-Prim. amyl	107°	0·901(0°)	129°	1·246(0°)	156°	1·543(0°)

Only the lower chlorides and methyl bromide are gaseous at the ordinary temperature, most of the others being liquids, and the highest members solids. The melting-points of some of these compounds have been determined accurately:

Alkyl-group.	Name.	Chloride.	Bromide.	Iodide.
CH_3	Methyl	−103·6°	− 96·8°	− 66·1°
C_2H_5	Ethyl	−140·85°	−119·0°	−110·9°
C_3H_7	*n*-Propyl	−122·5°	−109·85°	−101·4°

The densities of all the chlorides are less than 1, and diminish as the number of carbon atoms increases. The densities of the lower bromides and iodides are considerably greater than 1, although they also diminish with increase in the number of carbon atoms, the highest members of the homologous series being specifically lighter than water. All are very slightly soluble in water, but dissolve readily in many organic solvents. The lower members have a pleasant ethereal odour.

Chemical Properties.—In their action upon silver nitrate the alkyl halides differ very much from the halides of the metals. In aqueous or alcoholic solution the metallic halides yield at once a precipitate of silver halide, the reaction being quantitative. On the other hand, silver nitrate either does not precipitate silver halide from a solution of the alkyl halides, or the reaction is slow. The explanation is the same as that given in **51**, actions of the first type being ionic, and those of the second type molecular. It follows that there are either no halogen ions present in an alkyl-halide solution, or at least that their number is very small.

The alkyl halides can be converted into one another, a process exemplified by the formation of alkyl iodides through heating the corre-

sponding chlorides with potassium or calcium iodide. These reactions often are incomplete.

The alkyl iodides are employed chiefly for introducing alkyl-groups into organic compounds.

Alkyl fluorides are known also, and are more volatile than the corresponding chlorides. They are obtained by the action of silver fluoride on alkyl iodides, and in other ways.

Esters of Other Mineral Acids.

54. Esters of a great number of mineral acids are known. The general methods for their preparation are as follows:

1. By the action of the acid on the absolute alcohol:

$$\underset{\text{Alcohol}}{C_2H_5\cdot\boxed{OH+H}}\cdot\underset{\text{Nitric acid}}{ONO_2}=H_2O+\underset{\text{Ethyl nitrate}}{C_2H_5\cdot ONO_2}.$$

2. By the action of an alkyl halide on a silver salt:

$$SO_4\boxed{Ag_2+2I}C_2H_5=\underset{\text{Ethyl sulphate}}{SO_4(C_2H_5)_2}+2AgI.$$

3. By the action of mineral-acid chlorides on alcohols or alkoxides:

$$\underset{\substack{\text{Phosphorus}\\\text{oxychloride}}}{PO\boxed{Cl_3+3Na}OC_2H_5}=\underset{\substack{\text{Normal ethyl}\\\text{phosphate}}}{PO(OC_2H_5)_3}+3NaCl.$$

The acid esters of sulphuric acid are termed *alkylsulphuric acids*, and are of some importance. *Ethylsulphuric acid*, or *ethyl hydrogen sulphate*, $C_2H_5O\cdot SO_2\cdot OH$, is obtained by mixing alcohol with concentrated sulphuric acid. The formation of this compound is never quantitative, because the reaction attains an equilibrium (**93**). The alkylsulphuric acids are separated from the excess of sulphuric acid by means of their barium (or strontium or calcium) salts, these compounds being readily soluble in water, whilst the sulphates are wholly or almost insoluble. It is necessary only to neutralize the mixture of sulphuric acid and alkylsulphuric acid with barium carbonate, the product being a solution of barium ethylsulphate, $\begin{matrix}\text{ba}^*\\C_2H_5\end{matrix}>SO_4$. The free ethylsulphuric acid is obtained by the addition of the calculated quantity of sulphuric acid to this solution. At the ordinary temperature it is an odourless, oily, strongly acidic liquid, miscible with water in all proportions. The aqueous solution decomposes into sulphuric acid and alcohol, slowly at the laboratory temperature, but quickly at the boiling-point.

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* $\text{ba}=\frac{1}{2}\text{Ba}$.

Ethylsulphuric acid forms well-crystallized salts. Its potassium salt is employed in the preparation of ethyl compounds, an example being the ready formation of ethyl bromide through the dry distillation of a mixture of potassium bromide and potassium ethylsulphate:

$$\underset{\text{Potassium ethyl-sulphate}}{KO\cdot SO_2\cdot O\cdot \boxed{C_2H_5+Br}\, K} = \underset{\text{Potassium sulphate}}{KO\cdot SO_2\cdot OK} + \underset{\text{Ethyl bromide}}{C_2H_5Br}.$$

When free ethylsulphuric acid is heated, the neutral ethyl ester of sulphuric acid and free sulphuric acid are formed:

$$SO_2<\begin{matrix}OC_2H_5\\OH\end{matrix} + SO_2<\begin{matrix}OH\\OC_2H_5\end{matrix} = SO_2<\begin{matrix}OH\\OH\end{matrix} + SO_2<\begin{matrix}OC_2H_5\\OC_2H_5\end{matrix}.$$

Simultaneously, free sulphuric acid and ethylene are produced (115):

$$SO_2<\begin{matrix}OC_2H_5\\OH\end{matrix} = SO_2<\begin{matrix}OH\\OH\end{matrix} + C_2H_4.$$

The conversion of ethylsulphuric acid into ether is described in 56.

Dimethyl sulphate, $(CH_3)_2SO_4$, is obtained by the vacuum-distillation of methylsulphuric acid:

$$2CH_3HSO_4 = (CH_3)_2SO_4 + H_2SO_4.$$

It is an oily, very poisonous liquid, boiling at 188°, and often is employed in the introduction of methyl-groups into organic compounds.

Ethers.

55. The *ethers* are isomeric with the alcohols. Their constitution is proved by WILLIAMSON's synthesis, the action of an alkoxide on an alkyl halide:

$$C_nH_{2n+1}\cdot O\cdot \boxed{Na+I}\cdot C_mH_{2m+1} = C_nH_{2n+1}\cdot O\cdot C_mH_{2m+1} + NaI.$$

This synthesis affords confirmation of the view indicated in 39 as to the constitution of the alkoxides, the metal occupying the place of the alcoholic hydroxyl-hydrogen. The alternative possibility would be for the metal to have replaced a hydrogen atom in direct union with carbon, sodium methoxide having the formula $Na\cdot CH_2\cdot OH$. With ethyl iodide a compound of this type would yield propyl alcohol:

$$C_2H_5\cdot \boxed{I+Na}\cdot CH_2OH = C_2H_5\cdot CH_2OH + NaI.$$

This reaction does not take place. Methylethyl ether, with the empirical formula of an alcohol but none of its properties, is produced instead.

WILLIAMSON'S synthesis is possible also with a solution of the alkoxide in dilute alcohol (50 per cent.). Despite the presence of such a large proportion of water, the reaction is almost quantitative. It follows that the greater part of the substance must persist as sodium alkoxide, and not be decomposed by the water into alcohol and sodium hydroxide (50), since such decomposition would inhibit the formation of the ether.

56. The best-known compound of the homologous series of ethers is *diethyl ether*, $C_2H_5 \cdot O \cdot C_2H_5$, usually termed "ether." This compound is manufactured, and prepared in the laboratory also, from sulphuric acid and ethyl alcohol. For this purpose five parts of alcohol (90 per cent.) are heated with nine parts of concentrated sulphuric acid at a temperature between 130° and 140°. When ether and water begin to distil, alcohol is allowed to flow into the distillation-flask to keep the volume of liquid constant. Ether passes over continuously, but after about six times the initial volume of the alcohol in the acidic mixture has been added the proportion of alcohol in the distillate increases, and finally the formation of ether stops. Methylated spirit can be substituted for pure spirit, the product being designated "methylated ether."

The mechanism of the production of ether involves the initial formation of ethylsulphuric acid (54) from the alcohol and sulphuric acid. Ethylsulphuric acid can be decomposed by heating with water, sulphuric acid and the alcohol being regenerated:

$$C_2H_5 \cdot \boxed{OSO_3H + H}\, OH = C_2H_5 \cdot OH + H_2SO_4.$$

When ethyl alcohol instead of water reacts with ethylsulphuric acid, ether and sulphuric acid are formed in an exactly analogous manner:

$$C_2H_5 \cdot \boxed{O \cdot SO_3H + H} \cdot O \cdot C_2H_5 = C_2H_5 \cdot O \cdot C_2H_5 + H_2SO_4.$$

The production of ether depends on the formation of ethylsulphuric acid, and the subsequent decomposition of this compound into ethyl ether and sulphuric acid by the addition of more alcohol. Since in this reaction the sulphuric acid is regenerated, it yields a fresh quantity of ethylsulphuric acid, the process being continuous. Theoretically a small quantity of sulphuric acid could convert an unlimited amount of alcohol into ether, but in practice such efficiency is not attained. The

explanation lies in the generation of water as a by-product in the formation of ethylsulphuric acid from alcohol and sulphuric acid:

$$C_2H_5 \cdot \boxed{OH+H} SO_4H = C_2H_5 \cdot SO_4H + H_2O.$$

A part of this water distils along with the ether, but a part remains in the flask, and decomposes into alcohol and sulphuric acid the ethylsulphuric acid formed. When the proportion of water in the reaction-mixture exceeds a certain limit, it inhibits the formation of ethylsulphuric acid, and thus stops the production of ether.

When an alcohol other than ethyl alcohol is added to the original mixture shortly before distillation begins, a mixed ether is obtained:

$$C_2H_5 \cdot \boxed{SO_4H+H} \cdot O \cdot C_5H_{11} = C_2H_5 \cdot O \cdot C_5H_{11} + H_2SO_4.$$

This reaction proves the formation of ether to take place in the two stages indicated.

Senderens found that addition to the liquid of 5 per cent. of its weight of sulphate of either aluminium or lead induces the ready formation of ether at 120°.

The crude ether obtained by this method contains water, alcohol, and a small proportion of sulphur dioxide. It is left in contact with quicklime for several days, the water, sulphur dioxide, and part of the alcohol being thus removed. Subsequently it is distilled from a water-bath heated to about 55°. To remove the small proportion of alcohol remaining, it is extracted several times with small volumes of water, and the water is removed. The ether is separated from dissolved water by distillation, first over calcium chloride and finally over sodium.

Ethyl ether also is formed by passing alcohol-vapour over alum dehydrated at 195°. Its homologues also can be prepared by this method, although they are not produced by heating the corresponding alcohols with sulphuric acid, only unsaturated hydrocarbons of the series C_nH_{2n} being formed. Catalysis by alum of a mixture of alcohols affords a means of preparing mixed ethers.

Good yields of many simple and mixed ethers are obtained by the interaction of alkyl halides and alkoxides (112).

Diethyl ether is a colourless, very mobile liquid of agreeable odour. It boils at 35·4°, and solidifies at −117·6°. Prolonged breathing of it produces unconsciousness, followed by only slightly disagreeable after-effects. Ether therefore is employed in surgery as an anæsthetic. It is slightly soluble in water, one volume dissolving in 11·1 volumes of

water at 25°; water also dissolves slightly in ether (2 per cent. by volume at 12°). On account of its low boiling-point, ether is very volatile, and as its vapour is highly combustible and with air produces an explosive mixture, it is a substance requiring very careful handling. It burns with a luminous flame. Intense cold is produced by its evaporation, the outside of a flask containing it becoming coated with ice on promoting the evaporation of the ether by a rapid stream of air.

It is relatively difficult to induce reaction between ethers and chemical reagents. At ordinary temperatures they are unaffected by dilute acids, by alkalis, and by phosphorus pentachloride, and sodium does not eliminate hydrogen from them. When heated with hydrogen halides they do yield halogen derivatives. Gaseous hydrogen iodide can convert an ether at the ordinary temperature into the corresponding alcohol and alkyl iodide:

$$C_nH_{2n+1}\boxed{OC_mH_{2m+1}+H}I=C_nH_{2n+1}I+C_mH_{2m+1}OH.$$

Under the influence of heat the products are water and an alkyl iodide:

$$C_nH_{2n+1}\boxed{O}\boxed{C_mH_{2m+1}+2H}I=C_nH_{2n+1}I+C_mH_{2m+1}I+H_2O.$$

In the laboratory, ether is an invaluable solvent and crystallizing-medium for many compounds, and is utilized for extracting aqueous solutions (*23*). It is also of great service in many manufacturing processes.

COMPOUNDS CONTAINING ALKYL-RADICALS IN UNION WITH SULPHUR.

57. The elements in any individual group of the periodic system ("Inorganic Chemistry," **216–222**) yield similar compounds, a fact traceable to their having equal valencies: they also have similar chemical properties. Experience has shown organic compounds containing elements of such a group to display the properties of their inorganic analogues in every variety of similarity and dissimilarity, their points of resemblance and of difference being sometimes even more marked than those of the inorganic compounds. A comparison of the oxygen compounds hitherto considered with the sulphur compounds of similar structure will serve as an example.

The alcohols and ethers can be regarded as derived from water by the replacement of one or both of its hydrogen atoms by alkyl. The corresponding sulphur compounds are derived similarly from hydrogen sulphide, and are represented thus:

$$C_nH_{2n+1}\cdot SH \quad \text{and} \quad C_nH_{2n+1}\cdot S\cdot C_mH_{2m+1}.$$

The first are termed *mercaptans* or *thiols*, and the second *thioethers*.

The resemblance of these compounds to the alcohols and ethers is noticeable chiefly in their methods of formation, for if potassium hydrogen sulphide instead of potassium hydroxide react with an alkyl halide, a mercaptan is formed:

$$C_nH_{2n+1}\cdot \boxed{X+K}\cdot SH = C_nH_{2n+1}\cdot SH + KX.$$

Like the alcohols, the mercaptans have in the molecule only one hydrogen atom replaceable by metals. It is therefore reasonable to assume the hydrogen atom thus distinguished from all the others to be in union with sulphur, the other hydrogen atoms being attached to carbon.

The ethers are formed by the action of alkyl halides on alkoxides, and the thioethers are obtained analogously by combination of metallic compounds of the mercaptans, the *mercaptides* or *thiolates*, with alkyl halides:

$$C_nH_{2n+1}\cdot S\cdot \boxed{Na+I}\cdot C_mH_{2m+1} = C_nH_{2n+1}\cdot S\cdot C_mH_{2m+1} + NaI.$$

Water is a neutral compound, and hydrogen sulphide is a weak acid; in consequence alcohol does not form alkoxides with the bases of the heavy metals, whereas mercaptans yield mercaptides with them. An alcohol soluble with difficulty in water, such as amyl alcohol, does not dissolve in alkalis; but the mercaptans, although insoluble in water, dissolve readily in alkalis, forming mercaptides. They possess therefore an acidic character.

Thiols or Mercaptans.

58. The mercaptans can be obtained also by the action of phosphorus pentasulphide on alcohols:

$$5C_nH_{2n+1}\cdot OH + P_2S_5 \rightarrow 5C_nH_{2n+1}\cdot SH;$$

or by distilling a solution of potassium alkylsulphate with potassium hydrogen sulphide:

$$C_2H_5\cdot\boxed{O\cdot SO_3K + K\cdot}SH = C_2H_5\cdot SH + K_2SO_4.$$

They are liquids almost insoluble in water, with boiling-points markedly lower than those of the corresponding alcohols. Thus, *methyl mercaptan* or *methanethiol* boils at 6°, methyl alcohol at 66°, a striking phenomenon, sulphur being much less volatile than oxygen. It may be explained by assuming non-association of the mercaptan molecules, and association of the alcohol molecules. The mercaptans are distinguished by their exceedingly disagreeable odour, a property characteristic of almost all volatile sulphur compounds. Our olfactory organs are very sensitive to mercaptans, and can detect merest traces of them quite unrecognizable by chemical means. The smell of the perfectly pure mercaptans is much less objectionable than that of the crude products.

Many metallic compounds of the mercaptans are known, some of them in well-crystallized forms. The *mercury mercaptides* furnish an example of these bodies, and are produced by the action of mercaptans on mercuric oxide, whence the name of these compounds is derived (by shortening *corpus mercurio aptum* to *mercaptan*). Many other heavy metals, such as lead, copper, and bismuth, yield mercaptides: the lead compounds have a yellow colour. The mercaptan is liberated from all mercaptides by the addition of mineral acids.

Thioethers.

59. In addition to the methods given in 57 for the preparation of thioethers, the action of potassium sulphide, K_2S, on the salts of alkyl-sulphuric acids can be employed:

$$2C_2H_5\boxed{O\cdot SO_3K}+\boxed{K_2}S=(C_2H_5)_2S+2K_2SO_4.$$

Potassium ethylsulphate

The thioethers are neutral compounds with an exceedingly offensive odour, eliminated by heating with copper-powder. They are liquids insoluble in water, and yield double compounds with metallic salts, such as $(C_2H_5)_2S,HgCl_2$.

The interaction of ethylene and sulphur monochloride yields 2:2′-*dichlorodiethyl sulphide* in accordance with the equation

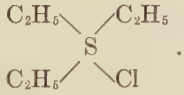
$$2C_2H_4+S_2Cl_2=(CH_2Cl\cdot CH_2)_2S+S.$$

In the war of 1914 to 1918 this substance was notorious as "mustard-gas." It is a liquid with a faint sweetish odour, and boils at 217°. Its vapour has a most destructive effect on the respiratory organs.

With one molecule of an alkyl iodide the thioethers form remarkable crystalline compounds of the type $(C_2H_5)_3SI$. These derivatives are termed *sulphonium iodides*, and are soluble readily in water. Moist silver oxide replaces the iodine atom by hydroxyl:

$$(C_2H_5)_3SI+AgOH=(C_2H_5)_3SOH+AgI.$$

The *sulphonium hydroxides* thus obtained dissolve easily in water, and are very alkaline in reaction. They are strong bases, absorbing carbon dioxide from the air, and yielding salts with acids. In the *sulphonium halides*, such as $(C_2H_5)S_3\cdot Cl$, sulphur being the only element capable of union with the univalent alkyl-groups and univalent chlorine atom, these substances must have constitutional formulæ of the type



The mercaptans resemble hydrogen sulphide in being oxidized slowly by contact with air, becoming converted into disulphides like *diethyl disulphide*,

$$C_2H_5\cdot S\cdot S\cdot C_2H_5.$$

The hydrogen attached to sulphur has been removed by oxidation, proving disulphides to have the constitution indicated. A further proof is their formation by heating potassium ethylsulphate with potassium disulphide, K_2S_2.

Inorganic compounds containing oxygen and sulphur exist, and in organic chemistry similar substances are known.

The *sulphoxides*, $\begin{matrix}C_nH_{2n+1}\\C_nH_{2n+1}\end{matrix}>SO$, are formed by the oxidation of thioethers with nitric acid. Their constitution is indicated by their ready reduction to thioethers. If the oxygen were linked to carbon, they would not behave in this manner, because neither alcohols nor ethers lose their oxygen through gentle reduction.

The *sulphones* are compounds with the constitution $\begin{matrix}C_nH_{2n+1}\\C_nH_{2n+1}\end{matrix}>SO_2$, as is proved in **60**. They are formed by energetic oxidation of the thioethers, and also by oxidizing sulphoxides. Nascent hydrogen is unable to effect their reduction.

Sulphonic Acids.

60. The *sulphonic acids* are produced from mercaptans by energetic oxidation with nitric acid. They have the formula $C_nH_{2n+1}\cdot SO_3H$. During the oxidation the alkyl-group remains intact, for the salts of these sulphonic acids are formed also by interaction of an alkyl iodide and a sulphite:

$$C_2H_5\boxed{I+K}SO_3K=KI+C_2H_5SO_3K.$$

Since the sulphur in mercaptans is in direct union with carbon, the sulphonic acids have an analogous constitution. Additional proof is furnished by the reduction of sulphonic acids to mercaptans. The structure of ethylsulphonic acid is therefore $CH_3\cdot CH_2\cdot SO_3H$.

The group SO_3H must contain a hydroxyl-group, because with a sulphonic acid phosphorus pentachloride yields a *sulphonyl chloride*, $C_nH_{2n+1}\cdot SO_2Cl$, capable of reconversion into the sulphonic acid through the action of water. The structure of the compound is therefore

$$CH_3\cdot CH_2\cdot SO_2\cdot OH.$$

The alkylsulphonic acids are strongly acidic, very hygroscopic, crystalline substances, and are very soluble in water.

In the sulphonyl chlorides, chlorine can be replaced by hydrogen in the nascent state. The derivatives obtained thus have the formula $C_nH_{2n+1}\cdot SO_2H$, and are termed *sulphinic acids*. When an alkyl halide reacts with the sodium salt of a sulphinic acid, a sulphone (**59**) is formed:

$$C_2H_5SO_2\boxed{Na+Br}C_2H_5=\begin{matrix}C_2H_5\\C_2H_5\end{matrix}>SO_2+NaBr.$$

This mode of preparation is a proof of the constitution of the sulphones.

Selenium and *tellurium* compounds corresponding with most of these sulphur compounds are known, and they also have a most offensive odour.

COMPOUNDS CONTAINING ALKYL-RADICALS IN UNION WITH NITROGEN.

I. AMINES.

61. At the beginning of the last chapter (**57**) the properties possessed by inorganic compounds were stated to be even more marked in their organic derivatives. The compounds described in this chapter afford another striking example of this phenomenon.

The term *amines* is applied to substances capable of being regarded as derived from ammonia by exchange of hydrogen for alkyl-radicals. The most characteristic property of ammonia is its power of combining with acids to form salts by direct addition:

$$NH_3+H\cdot X=NH_4\cdot X.$$

Thereby tervalent nitrogen is made quinquevalent, a change connected intimately with its basic character. This property is found also among the alkylamines. The early members of the series are even better conductors of electricity for the same molecular concentration of their aqueous solutions than ammonia, and are therefore more basic ("Inorganic Chemistry," **66** and **240**). Ammonium hydroxide, NH_4OH, a substance unknown in the free state except possibly at low temperature, exists in the aqueous solution of ammonia. It is very unstable, being decomposed completely into water and ammonia by boiling its solution. It has only weakly basic properties, because there are but few ammonium ions and hydroxyl-ions in its aqueous solution, apparently because the compound NH_4OH has a very strong tendency to break up into ammonia and water. Such a decomposition is not possible for compounds containing four alkyl-groups in place of the four hydrogen atoms of the ammonium radical, and experience has proved these compounds to possess great stability. Since the nitrogen cannot revert to the tervalent condition, their basic character, in comparison with that of ammonium hydroxide, is so strengthened that they are ionized to almost the same degree as the alkalis.

The table indicates the degree of ionization of some of these compounds, that of lithium hydroxide being taken as 100, the strength of the bases having been determined by the velocity of saponification of methyl acetate:

$LiOH$	100	$(C_2H_5)_2H_2N\cdot OH$	16
$NaOH$	98	$(C_2H_5)H_3N\cdot OH$	12
$(C_2H_5)_4N\cdot OH$	75	$H_4N\cdot OH$	2
$(C_2H_5)_3HN\cdot OH$	14		

The amines yield complex salts fully analogous to the platinum salt, $(NH_4)_2PtCl_6$, and the gold salt, NH_4AuCl_4, of ammonia.

Nomenclature and Isomerism.

62. In the nomenclature of the amines those with one nitrogen atom are regarded as ammonia having hydrogen replaced by alkyl, and not as alkanes with the NH_2-group substituted for hydrogen. All basic substances are denoted by the termination *ine*.

The amines are termed *primary*, *secondary*, or *tertiary*, in correspondence with the exchange for alkyl-radicals of one, two, or three hydrogen atoms of ammonia, NH_3. The compounds NR_4OH, R representing an alkyl-radical, are named *quaternary ammonium bases*.

Isomerism of the amines may be due to various causes. First, it may arise from branching of the carbon chain, just as in the alcohols and other compounds. Second, it may be due to the position occupied by the nitrogen in the molecule. Third, it may be caused by both causes simultaneously. In addition to these influences, the primary, secondary, and tertiary nature of the amines must be taken into account. A compound C_3H_9N, for example, can be propylamine or *iso*propylamine, $CH_3 \cdot CH_2 \cdot CH_2 \cdot NH_2$ or $\begin{matrix} CH_3 \\ CH_3 \end{matrix} > CH \cdot NH_2$, primary; methylethylamine, $\begin{matrix} CH_3 \\ C_2H_5 \end{matrix} > NH$, secondary; or trimethylamine, $\begin{matrix} CH_3 \\ CH_3 \\ CH_3 \end{matrix} > N$, tertiary.

Methods of Formation.

63. Hofmann discovered that heating an alcoholic or aqueous solution of ammonia with an alkyl halide induces the following reactions:

$$\text{I.} \quad C_nH_{2n+1} \cdot Cl + pNH_3 = C_nH_{2n+1} \cdot NH_2, HCl + (p-1)NH_3.$$

The alkyl halide forms an addition-product with ammonia, NH_3, a reaction analogous to the formation of ammonium chloride, NH_4Cl, from ammonia, NH_3, and hydrogen chloride, HCl. Part of the resulting hydrochloride is decomposed by ammonia, with liberation of the primary amine, the free base reacting with the alkyl halide in accordance with equation II:

$$\text{II.} \quad C_nH_{2n+1} \cdot Cl + C_nH_{2n+1} \cdot NH_2 = (C_nH_{2n+1})_2NH, HCl.$$

Part of the secondary amine thus produced is set free also, and reacts according to equation III:

$$\text{III.} \quad C_nH_{2n+1} \cdot Cl + (C_nH_{2n+1})_2NH = (C_nH_{2n+1})_3N, HCl.$$

The tertiary amine undergoes partial liberation, and reacts with the alkyl halide to yield the halide of a quaternary ammonium base:

$$\text{IV.} \quad (C_nH_{2n+2})_3N + C_nH_{2n+1} \cdot Cl = (C_nH_{2n+1})_4N \cdot Cl.$$

Excess of ammonia is assumed to be employed; but even when it is not, and in general for every proportion of alkyl halide and ammonia, the reaction is in these four phases. As a final result, the primary, secondary, and tertiary amines, and the ammonium base, are formed simultaneously. Often by adjusting the proportion of ammonia and alkyl halide, the duration of the reaction, and other conditions, it is possible to obtain a given amine as main product, the quantities of the other amines being relatively small. The nature of the alkyl-group also exerts a great influence on the character of the reaction-product.

The separation of the ammonium bases from the ammonia and amines is simple, the amines being liquids volatilizing without decomposition or gases, and the ammonium bases not being volatile. On distillation of the mixture of the amine hydrohalides and the ammonium bases after addition of potassium hydroxide, only the free amines pass over.

To separate the primary amines from the mixture of the hydrohalides of the three amines, fractional crystallization often is employed for the lower members, methylamine, dimethylamine, and so on. The propylamines and those succeeding can be separated by fractional distillation.

Various methods of preparing primary amines unmixed with secondary or tertiary amines are known (78, 96, 259, 268, and 349).

64. The *velocity of the formation of tetra-alkylammonium iodides* from triethylamine and an alkyl iodide or bromide has been investigated by Menschutkin. It has the character of a bimolecular reaction ("Inorganic Chemistry," 51) according with the equation

$$s = \frac{dx}{dt} = k(a-x)(b-x),$$

s being the velocity, k the constant of the reaction, a and b the quantities of amine and iodide per unit volume expressed in molecules, and x the quantity of both which has entered into reaction after the time t. Solution of this equation by the integral calculus gives

$$k = \frac{1}{t(a-b)} \times \log_e \frac{b(a-x)}{a(b-x)}.$$

For the investigation of these velocities, weighed quantities of the amine and iodide are brought into contact in a suitable solvent, and the solution is heated in a sealed tube at 100°, x being determined after the lapse of known intervals of time t. The value of k is found to be constant for every reaction; that is, if corresponding sets of values be substituted for t and x in the equation, on solving it the same value for k is obtained always. The greater the molecular weight of the alkyl-

radical, the smaller is k, although the decrease is not very marked: for example, when the amine reacts with propyl bromide, $k = 0{\cdot}00165$; with octyl bromide employing acetone as solvent $k = 0{\cdot}00110$. The equation is applicable normally, being independent of the solvent, a fact in accord with the absence of any term dependent on the nature of the solvent. Instances are known, however, of the extraordinary magnitude of the influence exerted by the solvent on the values of k. With hexane as solvent, for the interaction of triethylamine and ethyl iodide $k = 0{\cdot}000180$; but for methyl alcohol $k = 0{\cdot}0516$, or 286·6 times as great.

In many other instances the solvent exerts an important influence on the velocity of reaction, but a satisfactory explanation of the phenomenon is lacking.

Properties.

65. The primary, secondary, and tertiary amines are distinguished sharply by differences in their behaviour towards nitrous acid, HO·NO.

Primary amines yield alcohols, with evolution of nitrogen:

$$\begin{matrix} C_nH_{2n+1} \\ +OH \end{matrix}\boxed{\begin{matrix} N|H_2 \\ N|O \end{matrix}} = C_nH_{2n+1}\cdot OH + N_2 + H_2O.$$

The reaction is fully analogous to the decomposition of ammonium nitrite into water and nitrogen:

$$NH_3\cdot HONO = \boxed{\begin{matrix} H\cdot|N|H_2 \\ HO|N|O \end{matrix}} = 2H_2O + N_2.$$

Secondary amines yield *nitrosoamines*:

$$(C_nH_{2n+1})_2N\boxed{H+HO}NO = (C_nH_{2n+1})_2N\cdot NO + H_2O.$$

The lower members are yellowish liquids of characteristic odour, and are slightly soluble in water. They are reconverted easily into secondary amines by the action of concentrated hydrochloric acid (298). This reaction is a proof of the structure indicated, for direct union of the nitroso-group with carbon through either its oxygen or its nitrogen would eliminate the possibility of thus reconverting the nitrosoamine into a secondary amine.

Tertiary amines either are unaffected by nitrous acid, or suffer oxidation.

Their behaviour with nitrous acid affords therefore a means of distinguishing the three classes of amines. It serves also as a basis for the separation of the secondary and tertiary amines in the pure state from a mixture of the two types. Addition of a concentrated solution

of sodium nitrite to a hydrochloric-acid solution of a mixture of the two amines converts the secondary amine into a nitrosoamine in the form of an oil on the surface of the aqueous solution, and removable by means of a separating-funnel. The tertiary amine is not attacked, but remains in the aqueous solution in the form of a salt, and can be obtained by distilling with potassium hydroxide. During the process any primary amine present undergoes decomposition.

Another method of distinguishing primary, secondary, and tertiary amines consists in the determination of the number of alkyl-groups with which the amine can combine. For example, if a compound C_3H_9N be propylamine, $C_3H_7NH_2$, by heating with excess of methyl iodide it should yield a compound

$$\begin{matrix} C_3H_7 \\ (CH_3)_3 \end{matrix} NI = C_6H_{16}NI;$$

or if the formula $C_3H_9N = \begin{matrix} C_2H_5 \\ CH_3 \end{matrix} > NH$, similar treatment should yield $\begin{matrix} C_2H_5 \\ (CH_3)_3 \end{matrix} NI = C_5H_{14}NI$; or lastly, if $C_3H_9N = (CH_3)_3N$, there should be obtained $(CH_3)_4NI = C_4H_{12}NI$. A titration of the iodine ion of the quaternary ammonium iodide formed reveals the primary, secondary, or tertiary character of the compound C_3H_9N.

HOFMANN'S test for primary amines is described in **77.**

Individual Members.

66. The lower members are inflammable gases, and are very soluble in water, 1150 volumes of methylamine dissolving in one volume of water at 12·5°. The succeeding members have low boiling-points, and are miscible with water in all proportions. Both they and the lower members have a characteristic ammoniacal odour, like boiled lobsters. The higher members are odourless and insoluble in water. The densities of the amines are considerably less than 1, that of methylamine at −11° being only 0·699. The table indicates the variations in their boiling-points.

Alkyl-radical.	Primary.	Secondary.	Tertiary.
Methyl	−6°	7°	3·5°
Ethyl	19°	56°	90°
n-Propyl	49°	98°	156°
n-Butyl	76°	160°	215°
n-Octyl	180°	297°	366°

Methylamine is present in *Mercurialis perennis*, and is prepared readily by the interaction of ammonia and dimethyl sulphate. *Dimethylamine* (299) and *trimethylamine* are constituents of herring-brine.

Trimethylamine, $(CH_3)_3N$, can be prepared conveniently by heating ammonium chloride with formaldehyde ("Formalin," 108) in an autoclave at temperatures between 120° and 160°:

$$2NH_3+9CH_2O=2(CH_3)_3N+3CO_2+3H_2O.$$

Tetramethylammonium hydroxide, $(CH_3)_4N\cdot OH$, is obtained by the interaction of a solution of the corresponding chloride in methyl alcohol and the equivalent quantity of potassium hydroxide. After filtration of the precipitated potassium chloride, the solution is diluted with water, and evaporated *in vacuo* at 35° to remove the alcohol. The base crystallizes as very hygroscopic hydrates characterized by their ready absorption of carbon dioxide. It is decomposed by heat into trimethylamine and methyl alcohol:

$$(CH_3)_4N\cdot OH=(CH_3)_3N+CH_3OH.$$

The higher ammonium bases are converted by dry distillation into a tertiary amine, water, and a hydrocarbon C_nH_{2n}:

$$\underset{\text{Triethylamine}}{(C_2H_5)_3N}+\underset{\text{Ethylene}}{C_2H_4}$$

$$(C_2H_5)_4N\cdot OH=(C_2H_5)_3N+C_2H_4+H_2O.$$

The structure of the ammonium bases depends on the capacity of the nitrogen atom to unite with the four univalent alkyl-groups and the univalent hydroxyl-group. In view of its quinquevalency in these compounds, the constitution of the ammonium bases must be

$$\begin{matrix} C_nH_{2n+1} \\ C_mH_{2m+1} \\ C_pH_{2p+1} \end{matrix}\!\!>\!N\!<\!\begin{matrix} C_rH_{2r+1} \\ OH \end{matrix},$$

n, m, p, and r being similar or dissimilar.

67. Alkyl-derivatives of *hydrazine* or *diamide*, $H_2N\cdot NH_2$, are known. Among the methods for their preparation are the direct introduction of an alkyl-group into hydrazine, and the careful reduction of nitrosoamines (65). They have little power of resisting oxidizers, exemplified by their reduction of an alkaline copper solution at the ordinary temperature.

II. NITRO-COMPOUNDS.

68. By the interaction of silver nitrite and an alkyl iodide two compounds are formed, both having the empirical formula $C_nH_{2n+1}NO_2$, but different boiling-points. A typical example is the conversion of ethyl iodide into a substance $C_2H_5NO_2$ boiling at 17°, and another isomeride boiling at 113°–114°, the two substances being separable readily by fractionation.

The compound of lower boiling-point is decomposed into alcohol and nitrous acid by the action of potassium hydroxide, and therefore must be regarded as an ester of nitrous acid formed in accordance with the equation

$$C_nH_{2n+1}\boxed{I+Ag}\cdot ONO = C_nH_{2n+1}\cdot ONO + AgI.$$

Reduction transforms these esters or *alkyl nitrites* into an alcohol and ammonia.

The isomeride of higher boiling-point behaves quite differently. It is not converted into a nitrite and alcohol by the action of alkalis, and on reduction its two oxygen atoms are replaced by two hydrogen atoms with formation of a primary amine:

$$C_nH_{2n+1}NO_2 \rightarrow C_nH_{2n+1}NH_2.$$

The last reaction proves the nitrogen in this class of compound to be united directly with carbon as in the amines. The oxygen atoms can be attached only to the nitrogen, because the reduction to amine occurs at the ordinary temperature. Without the aid of heat it is not possible to replace oxygen in direct union with carbon, neither alcohols nor ethers being reduced at low temperatures to substances not containing oxygen. This fact indicates the constitution $C_nH_{2n+1}—NO_2$ for these *nitro-compounds.*

Nitro-compounds therefore contain the nitro-group, NO_2, *the nitrogen atom being in direct union with carbon.*

The generation of nitrite and nitro-compound may be explained by assuming the production of the nitrite to be a normal ionic reaction, and that of the nitro-compound to involve the preliminary formation of an addition-product, $\begin{matrix} Ag\cdot O\cdot N\cdot O \\ \diagup\quad\diagdown \\ I \qquad C_2H_5 \end{matrix}$, subsequently decomposed with fission of silver iodide. Confirmation of this view is furnished by the conversion by dimethyl sulphate of a dilute aqueous solution of potassium nitrite into methyl nitrite only, whereas a concentrated solution of the nitrite yields up to 25 per cent. of nitromethane.

The names of the nitro-compounds are formed from those of the saturated hydrocarbons by prefixing *nitro*, the compound CH_3NO_2 being *nitromethane*, $C_2H_5NO_2$ *nitroethane*, and so on. The members of the aliphatic homologous series are termed *nitroparaffins*. They are colourless liquids of ethereal odour, and the lower members are slightly soluble in water. All of them distil without decomposition.

69. The nitro-derivatives have a number of characteristic properties, among them the possession of one hydrogen atom replaceable by alkali-metals, especially sodium. This sodium compound is obtained most readily by the action of sodium ethoxide or methoxide on the nitro-compound in solution in absolute alcohol. A fine, white, crystalline precipitate is formed, that derived from nitroethane having the composition $C_2H_4NaNO_2$. The insolubility of these sodium compounds in absolute alcohol is employed sometimes in the separation of the nitroparaffins from other substances.

This power of exchanging hydrogen for sodium is conditioned by the presence of at least one hydrogen atom attached to the carbon atom carrying the nitro-group. As from nitroethane, a metallic compound is obtained from secondary nitropropane,

$$CH_3 \cdot CH < \begin{matrix} CH_3 \\ NO_2 \end{matrix};$$

but tertiary nitrobutane,

$$\begin{matrix} CH_3 \\ CH_3 \end{matrix} > C \cdot NO_2, \quad CH_3$$

does not yield a corresponding metallic derivative. The structure of these metallic compounds is considered in **322.**

Contact of an alkaline solution of a nitro-compound with bromine substitutes the halogen for one or more of the hydrogen atoms attached to the carbon atom carrying the nitro-group. This reaction is analogous to the substitution by metals, it being possible to introduce one additional bromine atom into $CH_3 \cdot CHBrNO_2$, but not into $CH_3 \cdot C \begin{matrix} Br \\ CH_3 \\ NO_2 \end{matrix}$.

70. The behaviour of nitro-compounds with nitrous acid is very characteristic, and affords a method of distinguishing primary, secondary, and tertiary nitro-derivatives. The reaction involves the addition of sodium nitrite to an alkaline solution of the nitro-compound, and acidification with dilute sulphuric acid. From a primary nitro-compound, an *alkylnitrolic acid* is formed:

$$CH_3 \cdot C \begin{matrix} \boxed{H_2 + O} \\ NO_2 \end{matrix} NOH = CH_3 \cdot C \begin{matrix} N \cdot OH \\ NO_2 \end{matrix} + H_2O.$$

Ethylnitrolic acid

The constitution of these compounds is indicated by their production from a dibromonitro-compound through the action of hydroxylamine, H_2NOH:

$$CH_3\cdot C\begin{array}{l}\boxed{Br_2+H_2}\,NOH\\ \diagdown NO_2\end{array}=CH_3\cdot C\begin{array}{l}\diagup\!\!\!\diagup NOH\\ \diagdown NO_2\end{array}+2HBr.$$

The alkylnitrolic acids dissolve in alkalis, yielding metallic compounds of blood-red colour, this reaction affording a characteristic test for them. They crystallize well, but are unstable.

A similar process transforms the secondary nitro-compounds into pseudo*nitroles*. They contain the group $=C<\begin{array}{l}NO\\ NO_2\end{array}$:

$$\begin{array}{l}CH_3\\ CH_3\end{array}>C<\begin{array}{l}\boxed{H+HO}\,NO\\ NO_2\end{array}=\begin{array}{l}CH_3\\ CH_3\end{array}>C<\begin{array}{l}NO\\ NO_2\end{array}+H_2O.$$

Propyl*pseudo*nitrole.

The solid *pseudo*nitroles are colourless, crystalline substances, but in the fused state or in solution they have an intense blue colour. This characteristic serves as a test for them.

Lastly, the tertiary nitro-compounds are unaffected by nitrous acid.

Among the other properties of nitro-compounds is their decomposition through heating with hydrochloric acid into the corresponding acid with the same number of carbon atoms and hydroxylamine:

$$\underset{\text{Nitroethane}}{CH_3\cdot CH_2\cdot NO_2}+H_2O=\underset{\text{Acetic acid}}{CH_3\cdot COOH}+\underset{\text{Hydroxylamine.}}{H_2NOH}.$$

The mechanism of this reaction is explicable on the assumption of the preliminary transformation of the nitro-compound into a *hydroxamic acid*:

$$R\cdot CH_2NO_2\rightarrow \underset{\text{Hydroxamic acid}}{R\cdot C\begin{array}{l}\diagup\!\!\!\diagup NOH\\ \diagdown OH\end{array}}.$$

The hydroxamic acid formed is converted into the acid and hydroxylamine by the water present:

$$R\cdot C\begin{array}{l}\diagup\!\!\!\diagup NOH\\ \diagdown OH\end{array}+H_2O=\underset{\text{Acid}}{R\cdot C\begin{array}{l}\diagup\!\!\!\diagup O\\ \diagdown OH\end{array}}+\underset{\text{Hydroxylamine}}{H_2NOH}.$$

COMPOUNDS CONTAINING ALKYL-RADICALS IN UNION WITH OTHER ELEMENTS.

I. COMPOUNDS CONTAINING ALKYL-RADICALS IN UNION WITH ELEMENTS OF THE NITROGEN GROUP.

71. Ammonia unites readily with acids to form salts. Phosphine, PH_3, also possesses this property, although the phosphonium salts, PH_4X, are decomposed even by water into an acid and phosphine. In arsine, AsH_3, stibine, SbH_3, and bismuthine, BiH_3, the basic character has disappeared.

Ammonia cannot be oxidized easily, and at the ordinary temperature it is unaffected by the oxygen of the atmosphere. In contrast, the hydrides of phosphorus, arsenic, antimony, and bismuth are oxidized readily.

All these properties characterize the compounds of these elements with alkyl-radicals.

Phosphines.

72. The amines yield stronger bases than ammonia, and the *phosphines* form stronger bases than phosphine. In both types this property becomes more marked with increase in the number of alkyl-groups replacing hydrogen atoms, the salts of the monoalkylphosphines being decomposed by water, but not those of the dialkylphosphines and trialkylphosphines. The *quaternary phosphonium bases*, PR_4OH, are as strongly basic as the ammonium bases. When a phosphonium base is heated, it does not decompose like an ammonium base (66) into an alcohol (or $C_nH_{2n}+H_2O$) and a trialkyl base, but into a hydrocarbon C_nH_{2n+2} and an oxygen compound:

$$(C_2H_5)_4P\cdot OH = C_2H_6 + (C_2H_5)_3PO.$$

This derivative is termed *triethylphosphine oxide*. In this reaction the great affinity between phosphorus and oxygen plays an important part, as is indicated also by the ready oxidation of the phosphines, a change effected even by the action of the air. Nitric acid oxidizes phosphine, PH_3, to phosphoric acid, $OP(OH)_3$; and in an analogous manner the phosphines take up one oxygen atom, and in addition a number of oxygen

atoms equal to that of the hydrogen atoms in direct union with phosphorus:

$$\begin{matrix}CH_3\\H_2\end{matrix}P \text{ gives } \underset{\text{Monomethylphosphinic acid}}{\begin{matrix}CH_3\\(HO)_2\end{matrix}P{:}O}; \quad \begin{matrix}(CH_3)_2\\H\end{matrix}P \text{ gives } \underset{\text{Dimethylphosphinic acid}}{\begin{matrix}(CH_3)_2\\HO\end{matrix}P{:}O};$$

$$\text{and } (CH_3)_3P \text{ gives } \underset{\text{Trimethylphosphine oxide}}{(CH_3)_3P{:}O}.$$

The constitution of these compounds is established by a variety of considerations, exemplified by the dibasicity of the *monoalkylphosphinic acids*, the monobasicity of the *dialkylphosphinic acids*, and the lack of acidic properties displayed by the *trialkylphosphine oxides*.

The phosphines are colourless liquids of penetrating, stupefying odour. Methylphosphine, CH_3PH_2, is a gas: in very small quantities triethylphosphine has an odour of hyacinths.

Methods of Formation.—Only tertiary phosphines and phosphonium compounds are formed by the action of alkyl halides on phosphine, PH_3. Primary and secondary phosphines are obtained by heating phosphonium iodide, PH_4I, with an alkyl iodide and zinc oxide.

Arsines.

73. The *primary* and *secondary arsines*, H_2AsCH_3 and $HAs(CH_3)_2$, are produced by reduction of monomethylarsinic acid and dimethylarsinic acid, $(CH_3)HAsO{\cdot}OH$ and $(CH_3)_2AsO{\cdot}OH$, with amalgamated zinc-dust and hydrochloric acid. Each is oxidized immediately by the air. With water *tertiary arsines* do not yield bases. They are formed by the action of a zinc alkide on arsenic chloride, $AsCl_3$, and from sodium arsenide and an alkyl iodide:

$$AsNa_3+3C_2H_5I=As(C_2H_5)_3+3NaI.$$

Quaternary arsonium bases are characterized by the possession of strongly marked basic properties. They are prepared by the addition of alkyl halides to tertiary arsines, followed by the action on the resulting halide of silver hydroxide.

The best-known arsenic derivatives containing alkyl-radicals are the *cacodyl compounds*. They were investigated by Bunsen, and he gave them this name in consequence of their offensive smell. They are very poisonous. The term *cacodyl* is applied to the univalent group $\begin{matrix}CH_3\\CH_3\end{matrix}>As—$.

Cacodyl oxide, $[(CH_3)_2As]_2O$, is formed by distilling arsenious oxide with the acetate of an alkali-metal. All the other cacodyl compounds are obtained from cacodyl oxide, *cacodyl chloride*, $(CH_3)_2AsCl$, being prepared by heating the oxide with hydrochloric acid, and *cacodyl*, $(CH_3)_2As{\cdot}As(CH_3)_2$, by heating the chloride with zinc in an atmosphere of carbon dioxide. Contact with air causes spontaneous ignition of both compounds.

II. COMPOUNDS CONTAINING ALKYL-RADICALS IN UNION WITH THE ELEMENTS OF THE CARBON GROUP.

74. Like carbon, the elements silicon, germanium, tin, and lead are quadrivalent. Numerous attempts have been made to prepare compounds containing chains of silicon atoms resembling the carbon chains. They have not been successful, no compounds containing a chain of more than three silicon atoms having been prepared. So far as is at present known, silicon lacks the power of forming long chains like those present in many carbon compounds. On account of this defect, a "Chemistry of Silicon" analogous to the "Chemistry of Carbon" is not possible, the phenomenon having a threefold origin:

(1) The linking between silicon atoms (Si—Si) is endothermic, whereas that between carbon atoms (C—C) is exothermic.

(2) Most organic silicon compounds are decomposed readily by both water and oxygen.

(3) Such compounds are very subject to polymerization, with formation of amorphous powders.

Introduction of a single silicon atom into organic substances containing many carbon atoms produces derivatives of a character differing little from the corresponding carbon compounds, a fact exemplified by the existence of *tetraethylmonosilane*, $Si(C_2H_5)_4$, and *tetraethylmethane* or 3:3-*diethylpentane*, $C(C_2H_5)_4$. Each is a liquid, and is unaffected by either fuming nitric acid or fuming sulphuric acid at the ordinary temperature, but each yields substitution-products with chlorine. *Triethylmonosilane*, $(C_2H_5)_3SiH$, has a petroleum-like odour, a resemblance to *triethylmethane* or 3-*ethylpentane*, $(C_2H_5)_3CH$.

III. METALLIC ALKIDES.

75. When excess of ethyl iodide is warmed with zinc, a white crystalline compound, C_2H_5ZnI, is formed, and on stronger heating it yields *zinc ethide*, $Zn(C_2H_5)_2$, and zinc iodide:

$$2C_2H_5ZnI = Zn(C_2H_5)_2 + ZnI_2.$$

Zinc ethide can be separated by distillation, an operation necessitating the employment of an apparatus filled with an inert gas, because like the other zinc alkides this compound burns spontaneously on exposure to air.

The metallic alkides are colourless liquids, heavier than water. Zinc methide boils at 46°, zinc ethide at 118°, and zinc propide at 146°.

The interaction of an alkyl iodide and a zinc alkide yields a saturated hydrocarbon:

$$\begin{matrix} CH_3 \\ CH_3 \end{matrix} > \boxed{Zn + \begin{matrix} I \\ I \end{matrix}} \begin{matrix} \cdot CH_3 \\ \cdot CH_3 \end{matrix} = ZnI_2 + 2CH_3 \cdot CH_3.$$

Water converts zinc alkides into saturated hydrocarbons and zinc oxide:

$$Zn(CH_3)_2 + H_2O = 2CH_4 + ZnO.$$

The halogens react very energetically with zinc alkides, yielding alkyl halides.

Sodium alkides of the type of *sodium methide*, $CH_3 \cdot Na$, are formed by the interaction of sodium and mercury alkides. They are colourless, amorphous powders, are not dissolved by indifferent solvents, and ignite spontaneously on contact with air.

Very remarkable compounds of magnesium were obtained first by GRIGNARD. When magnesium-turnings are brought into contact with a dry ethereal solution of an alkyl iodide, one gramme-molecule of the halide being employed for each gramme-atom of magnesium, there ensues a reaction evolving sufficient heat to raise the ether to the boiling-point. When sufficient ether is present, all the magnesium dissolves, forming an *alkyl magnesium iodide*, $C_nH_{2n+1} \cdot Mg \cdot I$. This derivative is combined with one molecule of ether, for evaporation to dryness leaves a residue containing equimolecular proportions of ether and the metallic compound.

The alkyl magnesium halides of the type $R \cdot Mg \cdot X$ can be obtained free from ether by dissolving the alkyl halide in benzene, light petroleum, or other solvents, adding magnesium, and inducing the reaction by the introduction as a catalyst of a small proportion of a tertiary amine or of ether.

Unlike the zinc alkides, the alkyl magnesium halides do not ignite spontaneously on contact with air. They are employed often for syntheses, notably for those of the secondary and tertiary alcohols (**102**).

The alkyl magnesium halides are decomposed by water, with formation of saturated hydrocarbons:

$$C_nH_{2n+1} \cdot Mg \cdot Cl + H_2O = C_nH_{2n+2} + Mg(OH)Cl.$$

With hydrogen peroxide they yield primary alcohols:

$$R \cdot CH_2X + H_2O_2 = R \cdot CH_2OH + Mg(OH)X.$$

Mercury alkides are prepared similarly to zinc alkides. They do not ignite in the air, are not attacked by water, and are dangerously poisonous. Such compounds as $C_2H_5 \cdot Hg \cdot OH$ are weak bases.

Alkyl-derivatives of glucinum, magnesium, cadmium, aluminium, thallium, and lead have been obtained also, some by the aid of GRIGNARD'S alkyl magnesium halides. A typical instance is the formation of tin ethide by the interaction of stannic bromide and ethyl magnesium bromide:

$$SnBr_4 + 4C_2H_5 \cdot Mg \cdot Br = Sn(C_2H_5)_4 + 4MgBr_2.$$

CARBONITRILES AND *ISO*CARBONITRILES.

76. Distillation of potassium ethylsulphate with potassium cyanide or anhydrous potassium ferrocyanide, $K_4Fe(CN)_6$, produces a liquid of exceedingly unpleasant odour. By fractional distillation it can be separated into two substances, both with the formula C_3H_5N. One is termed *ethylcarbylamine*, and is present only in small proportion: it boils at 82°, and has a disagreeable smell like that of the original mixture. The other constitutes the main portion, and is named *ethyl cyanide*: it boils at 97°, and after purification has an odour of not unpleasant character and much less penetrating than that of ethylcarbylamine.

With inorganic acids these isomerides yield quite different decomposition-products. Ethylcarbylamine is attacked at the ordinary temperature, the oily layer floating on the surface of the acid dissolving completely, and the disagreeable odour disappearing. *Formic acid*, CH_2O_2, can be obtained from the solution by distillation; and on addition of potassium hydroxide to the residue in the distilling-flask and subsequent distillation, ethylamine, $C_2H_5NH_2$, passes over, indicating the nitrogen atom in ethylcarbylamine, C_3H_5N, to be united directly with the ethyl-group:

$$\underset{\substack{\text{Ethylcarbylamine}\\ \text{or Ethane}iso\text{carbonitrile}}}{C_3H_5N} + 2H_2O = \underset{\text{Formic acid}}{CH_2O_2} + \underset{\text{Ethylamine}}{C_2H_5NH_2}.$$

At the ordinary temperature ethyl cyanide is attacked somewhat slowly by inorganic acids, but heating accelerates their action. On warming the mixture in a flask with a reflux-condenser and subsequently distilling, *propionic acid*, $C_3H_6O_2$, passes over. This acid contains the same number of carbon atoms as ethyl cyanide, C_3H_5N. On making the residue in the flask alkaline and distilling again, ammonia is obtained, proving the nitrogen atom in ethyl cyanide not to be in direct union with the ethyl-group:

$$\underset{\text{Ethyl cyanide}}{C_3H_5N} + 2H_2O = \underset{\text{Propionic acid}}{C_3H_6O_2} + NH_3.$$

These facts indicate the nitrogen atom in ethylcarbylamine to be in direct union with the ethyl-group, and the three carbon atoms not to be united directly, for one of them can be eliminated with production of formic acid. In contrast, ethyl cyanide must have a chain of three carbon atoms like that in propionic acid (80), and the nitrogen cannot be attached directly to the ethyl-group. These facts are expressed by the constitutional formulæ

$$\underset{\text{Carbylamine}}{\text{I. } C_2H_5—NC}, \qquad \underset{\text{Cyanide}}{\text{II. } C_2H_5—CN}.$$

On account of their method of formation, each substance must contain the group CN.

Compounds with a structural formula like I are named *carbylamines* or iso*carbonitriles*; those with a structural formula like II are termed *cyanides* or *carbonitriles*. The names of the carbylamines are derived from their alkyl-radical, thus *methylcarbylamine*, *ethylcarbylamine*, and so on. The cyanides can be designated analogously *methyl cyanide*, *ethyl cyanide*, etc.; but usually they are termed *nitriles*, and are named after the corresponding acid. Thus $CH_3 \cdot CN$ is *acetonitrile*, and $C_2H_5 \cdot CN$ *propionitrile*, the homologues having analogous titles.

The constitution of the groups —CN and —NC requires further consideration. They are represented as —C≡N and —N=C, the first with a triple bond and the second with a double bond between carbon and nitrogen (*cf.* 119).

In Nef's view, the carbylamines furnish one of the few examples of compounds with a bivalent carbon atom. He proved the formula $R \cdot N : C$ to represent the constitution of the carbylamines by demonstrating addition of halogens, hydrogen halides, sulphur, and other substances to take place only at the carbon atom, with formation of compounds of such types as $R \cdot NCX_2$, $R \cdot NCHX$, and $R \cdot NCS$ (*cf.* 130 and 261).

*iso*Carbonitriles or Carbylamines.

77. Carbylamines are the principal product of the interaction of alkyl iodides and silver cyanide. They can be obtained unmixed with nitriles by the action of potassium hydroxide and chloroform, $CHCl_3$, on primary amines:

$$C_2H_5N\boxed{H_2}+C\boxed{HCl_3}+3KOH=3KCl+3H_2O+C_2H_5 \cdot NC.$$

The disagreeable and characteristic odour of the carbylamines makes this reaction an exceedingly delicate test for primary amines. Secondary and tertiary amines are not converted into carbylamines

by it, for they lack two hydrogen atoms in direct union with the nitrogen atom of the amine.

The carbylamines are colourless liquids, very stable towards alkalis, but converted readily by acids into a primary amine and formic acid. With dry hydrogen chloride in ethereal solution they yield unstable addition-products, such as $2CH_3NC,3HCl$.

Carbonitriles.

78. Carbonitriles constitute the chief product of the interaction of potassium cyanide and alkyl iodides (*cf.* 77). They are prepared also by the dry distillation of potassium cyanide and potassium alkylsulphate. Sometimes anhydrous potassium ferrocyanide, $K_4Fe(CN)_6$, can be substituted advantageously for potassium cyanide.

Carbonitriles are formed also by passing esters mixed with ammonia over oxide of aluminium or of thorium heated to a temperature between 480° and 500°:

$$R\cdot COOR' + NH_3 = R\cdot CN + R'\cdot OH + H_2O.$$

Other methods of preparation are mentioned in **96** and **103**.

The carbonitriles are liquids of characteristic odour, soluble in water, and having densities approximating to 0·8. They are converted by acids, and also by warming with alkalis, into fatty acids with the same number of carbon atoms and ammonia, a process termed *hydrolysis*. With many substances they form addition-products by conversion of the triple bond between nitrogen and carbon into a single bond, exemplified by the addition of nascent hydrogen in MENDIUS's reaction:

$$C_2H_5\cdot CN + 4H = C_2H_5\cdot CH_2\cdot NH_2.$$

This reduction is effected by passing a mixture of the vapour of a carbonitrile with hydrogen over finely-divided nickel or copper at 180° to 200°.

On raising the temperature to one between 320° and 330°, the primary amines are converted into the corresponding carbonitriles by elimination of hydrogen, the reaction with *iso*amylamine and certain other amines being almost quantitative.

A description of other addition-products of the carbonitriles is given in **97**.

ACIDS, $C_nH_{2n}O_2$.

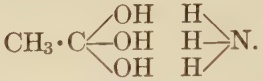
79. An addition-product is formed by the interaction of GRIGNARD'S alkyl magnesium halides (**75**) and carbon dioxide. Since magnesium exhibits great affinity for oxygen, this reaction can be explained by assuming the release from the alkyl-radical of the group—MgX, X representing halogen; and its subsequent union with an oxygen atom of the carbon dioxide, $C\begin{matrix}O\\O\end{matrix}$ being converted into $-C\begin{matrix}O\\OMgX\end{matrix}$. As this new group and the alkyl-radical previously attached to the group —MgX have one free carbon bond apiece, the two groups may be assumed to unite to form a compound $C_nH_{2n+1}-C\begin{matrix}O\\OMgX\end{matrix}$. This addition-product is decomposed by water, yielding an acid:

$$C_nH_{2n+1}-C\begin{matrix}O\\OMgX\end{matrix}+H_2O=C_nH_{2n+1}-C\begin{matrix}O\\OH\end{matrix}+Mg\begin{matrix}OH\\X\end{matrix}.$$

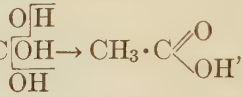
In accordance with these reactions the acids $C_nH_{2n}O_2$ contain the group $-C\begin{matrix}O\\OH\end{matrix}$ in union with an alkyl-radical. This view is supported by the formation of these compounds by other methods.

Among them is their synthesis by the interaction of an alkyl iodide and potassium cyanide, followed by hydrolysis of the carbonitrile formed. This hydrolysis consists in the addition of the elements of water, and entails breaking the bonds between carbon and nitrogen in the group $-C\equiv N$. If any other bond in a carbonitrile $CH_3\cdot CH_2\cdot CH_2 \ldots . CN$ were released, it would involve a severance of the carbon chain, and prevent the formation of an acid containing the same number of carbon atoms as the carbonitrile. The hydrolysis of the carbonitrile to form an acid and ammonia can be explained therefore by assuming the molecules of water to be resolved into hydroxyl and hydrogen, the hydroxyl uniting with the carbon, and the hydrogen with the nitrogen. By a threefold repetition of this hydrolysis the nitrogen is converted into

ammonia, the three bonds in the carbonitrile between carbon and nitrogen being severed:

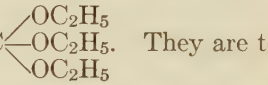


The formula of the acid produced is not $CH_3 \cdot CO_3H_3$, but $CH_3 \cdot CO_2H$, containing one molecule of water less. Elimination of one molecule of water from $CH_3 \cdot CO_3H_3$ yields



a substance containing the *carboxyl-group.*

In this explanation of the formation of acids, the existence of an intermediate compound with three hydroxyl-groups is assumed. Such substances are not known, but the assumption seems not improbable, because compounds containing three alkoxyl-groups exist, exemplified by the derivative



They are termed *ortho-esters* (**149**).

The acids $C_nH_{2n}O_2$ can be produced by the action of carbon monoxide on metallic alkoxides under the influence of heat:

$$CH_3 \cdot ONa + CO = CH_3 \cdot COONa.$$

The formation of an addition-product between $CH_3 \cdot ONa$ and CO can be explained by assuming the alkoxide to decompose first into CH_3 and ONa.

The conversion by oxidation of the primary alcohols into acids of the general formula $C_nH_{2n}O_2$ with the same number of carbon atoms in the molecule is mentioned in **45** and **46**. In this reaction the group $—CH_2OH$ becomes oxidized to —COOH.

The higher primary alcohols also can be transformed into the corresponding acids by heating with soda-lime, free hydrogen being evolved:

$$\underset{\text{Stearyl alcohol}}{C_{17}H_{35} \cdot CH_2OH} + NaOH = \underset{\text{Sodium stearate}}{C_{17}H_{35} \cdot COONa} + 2H_2.$$

Other methods are described in **98**, **145**, **164**, **232**, and **233**.

The presence of hydroxyl in the carboxyl-group is proved by the action of the chlorides of phosphorus, the hydroxyl-group being replaced by chlorine as with the alcohols.

In each molecule of the acids of this series there is one hydrogen atom replaceable by metals. Only the carboxyl-hydrogen atom is in

direct union with oxygen, and its special position suggests it to be the replaceable atom. The truth of this supposition has been proved by the interaction of silver acetate, $C_2H_3O_2Ag$, and ethyl iodide. Ethyl acetate is formed, whereas butyric acid would be produced from a compound with its silver atom attached to the methyl-carbon atom as in $CH_2Ag \cdot COOH$.

80. At the ordinary temperature the lower members of this series of acids are liquid. They can be distilled without decomposition, and in the concentrated state they have a very irritating and strongly acidic odour. They are miscible with water in all proportions. The middle members (C_4 to C_9) have a disagreeable rancid smell. They are of an oily nature, and do not mix with water in all proportions. At the ordinary temperature the higher members, beginning with C_{10}, are solid, are without odour, and in character resemble paraffin-wax. They are almost insoluble in water, and at the atmospheric pressure they cannot be distilled without decomposition. All the acids of this series dissolve readily in alcohol and ether. Except the first member, they are very stable towards oxidizers.

The acids of the series $C_nH_{2n}O_2$ are termed *fatty acids*, some of the higher members having been obtained first from fats. Their generic name is formed by adding "Carboxylic acid" to the name of the alkanes, the carboxyl-group being regarded as a substituent. Propionic acid is *ethanecarboxylic acid*, caprylic acid is *heptanecarboxylic*-1 *acid*, and so on.

Many of the fatty acids are natural products, occurring either in the free state or as esters, and are of great theoretical and technical importance. The table contains the names, formulæ, and certain physical constants of the normal-chain acids of the series:

Name.	Formula.	Melting-point.	Boiling-point.	Density.
Formic acid	CH_2O_2	8·3°	101°	1·2310 (10°)
Acetic acid	$C_2H_4O_2$	16·671°*	118°	1·0532 (16°)
Propionic acid	$C_3H_6O_2$	−22°	141°	0·9985 (14°)
Butyric acid	$C_4H_8O_2$	− 3·12°	162°	0·9599 (19·1°)
Valeric acid	$C_5H_{10}O_2$	−58·5°	186°	0·9560 (0°)
Caproic acid	$C_6H_{12}O_2$	− 1·5°	205°	0·9450 (0°)
Heptylic acid	$C_7H_{14}O_2$	−10·5°	223°	0·9186 (17·2°)
Caprylic acid	$C_8H_{16}O_2$	16·5°	237·5°	0·9100 (20°)
Nonylic acid	$C_9H_{18}O_2$	12·5°	254°	0·9110 (M.P.)
Capric acid	$C_{10}H_{20}O_2$	31·4°	269°	0·930 (37°)
Palmitic acid	$C_{16}H_{32}O_2$	62·618°	269° †	——
Margaric acid	$C_{17}H_{34}O_2$	60°	277° †	——
Stearic acid	$C_{18}H_{36}O_2$	69·32°	287° †	——

* At 760 mm. † At 100 mm.

Although the boiling-points rise with increase in the number of carbon atoms in the molecule, the melting-points of the acids with an

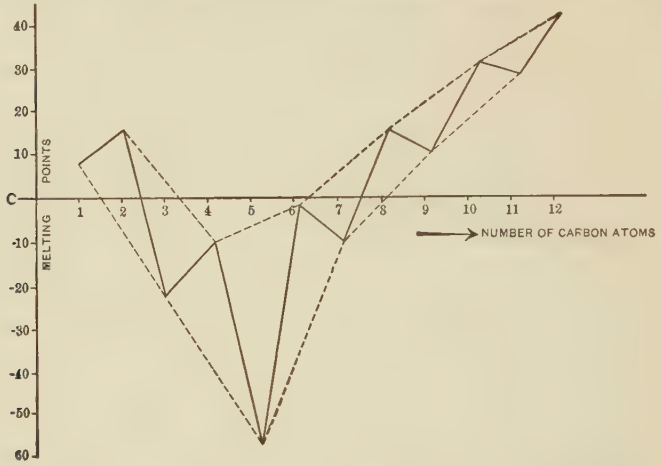


Fig. 27.—Melting-point Curve of the Fatty Acids.

even number of carbon atoms are higher than those of the acids immediately preceding and succeeding them, with an odd number of carbon atoms (Fig. 27). This phenomenon has been observed with other homologous series.

The groups which would remain on elimination of hydroxyl from fatty-acid molecules are unknown in the free state, but are named after the corresponding acids by changing the termination "ic" into "yl":

H·CO, Formyl;
CH_3·CO, Acetyl or Methanecarbonyl;
C_2H_5·CO, Propionyl or Ethanecarbonyl;
C_3H_7·CO, Butyryl or Propanecarbonyl;
C_4H_9·CO, Valeryl or Butanecarbonyl; etc.

Formic Acid, H·COOH.

81. *Formic acid* derives its name from its presence in the organism of ants (Latin, *formica*). It is manufactured by passing carbon monoxide at a pressure of eight atmospheres over soda-lime at 210°; and formate is produced also by the interaction of potassium hydrogen carbonate and hydrogen at a pressure of sixty atmospheres and a temperature of 70°. Palladium-black must be employed as a catalyst.

Moissan discovered a mode of synthesis from carbon dioxide and potassium hydride:

$$K\cdot H+CO_2+H\cdot COOK.$$

A convenient laboratory method for the production of formic acid is described in 163. Formic esters can be prepared by the interaction of carbon monoxide and alcohols under pressure, with alkoxides as catalysts:

$$R\cdot OH + CO = H\cdot COOR.$$

The acid can be obtained also by the oxidation of methyl alcohol.

Pure formic acid is a colourless liquid of irritating odour. Its salts are termed *formates*, and are soluble in water, some only with difficulty.

Formic acid is distinguished from its homologues by its susceptibility to oxidation and its consequent reducing power, and also by its ready decomposition. Addition of mercuric oxide to a solution of formic acid yields a solution of mercuric formate. By filtering this solution and warming the filtrate, mercurous formate is precipitated with evolution of carbon dioxide; on further warming, metallic mercury is liberated:

$$Hg\begin{matrix}OOCH & H\,COO\\ \boxed{OOCH + H|COO}\end{matrix}\ Hg = \underset{\text{Mercurous formate}}{2HgOOCH} + CO_2 + HCOOH;$$

Mercuric formate

$$Hg\ \underset{\text{Mercurous formate}}{\boxed{OOCH + H|COO}}\ Hg = 2Hg + CO_2 + HCOOH.$$

In this process half of the formic acid in the salt is set free, and half is oxidized. When a solution of silver formate is warmed, an exactly analogous reaction ensues; metallic silver is precipitated, carbon dioxide is evolved, and half of the acid is liberated.

Formic acid is capable of undergoing two types of decomposition:

$$\text{I. } H\cdot COOH \rightarrow H_2O + CO; \qquad \text{II. } H\cdot COOH \rightarrow H_2 + CO_2.$$

Decomposition I is induced by warming the acid with concentrated sulphuric acid, or by passing its vapour over heated tungsten pentoxide, W_2O_5, aluminium oxide, Al_2O_3, or silica, SiO_2. Other catalysts, such as finely-divided copper, nickel, stannous oxide (SnO), and zinc oxide (ZnO), cause decomposition in accordance with scheme II.

Under the influence of ultraviolet light of 2500 to 3000 Ångström units, formic acid in aqueous solution decomposes according to both schemes I and II, but the extent of the decomposition in accordance with II is approximately six times as great as that in accordance with I. When the solution is very concentrated, the evolved hydrogen reduces the carbon monoxide to *methanal* (108).

Obviously the properties of formic acid differ somewhat from those

of the other acids of the homologous series in which it is the first member. A similar phenomenon is of frequent occurrence.

Acetic or Methanecarboxylic Acid, $CH_3 \cdot COOH$.

82. *Acetic acid* has been known longer than any other acid. It is manufactured by two different methods.

a. By oxidation to vinegar of dilute alcohol, wine, beer, etc., through exposure to the air. The oxygen of the atmosphere oxidizes the alcohol by the aid of bacteria, the process being regulated to enable these bacteria to produce the greatest possible effect. To this end it is important for the temperature to be kept between 20° and 35°.

In the "quick" process for the preparation of vinegar (Fig. 28), dilute alcohol (6 to 10 per cent.) is allowed to drop on beechwood shavings contained in a vat with a perforated false bottom *a*. Holes in the side of the vat near the bottom serve to admit an ascending stream of air, opposite in direction to that of the alcohol. The shavings distribute the liquid over a very large surface, thus facilitating oxidation by the air, and at the same time they serve as a feeding-ground for the bacteria.

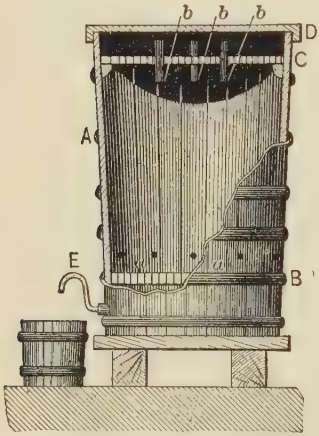


FIG. 28. — PREPARATION OF VINEGAR BY THE "QUICK" PROCESS.

b. Acetic acid is obtained in the distillation of wood (42). By means of quicklime, the acid is converted into calcium acetate and is freed from tarry impurities by heating to 200° in the air. The acetic acid is liberated by distilling with an equivalent quantity of concentrated hydrochloric acid. It can be purified by distillation from potassium dichromate, being very stable towards oxidizers.

A synthetic method for the preparation of acetic acid is now in operation (126). KOLBE's synthesis of acetic acid is described in 177.

At temperatures below 16·671° and a pressure of 760 mm., anhydrous acetic acid is solid and has the appearance of ice, hence the name *glacial* acetic acid. The solid acid has a penetrating odour, and is obtained by allowing a very concentrated solution of acetic acid to solidify, pouring off the liquid residue, melting the solidified acid, again allowing it to crystallize, and so on, these operations being repeated until the melting-point is constant. A rise of temperature and contraction of volume occur on mixing glacial acetic acid with water, the

maximum rise and contraction being produced with the proportion of one gramme-molecule of acetic acid to one gramme-molecule of water. This fact indicates the existence of a compound termed *ortho-acetic acid* (**79**), with the formula

$$CH_3 \cdot COOH \cdot H_2O = CH_3 \cdot C(OH)_3.$$

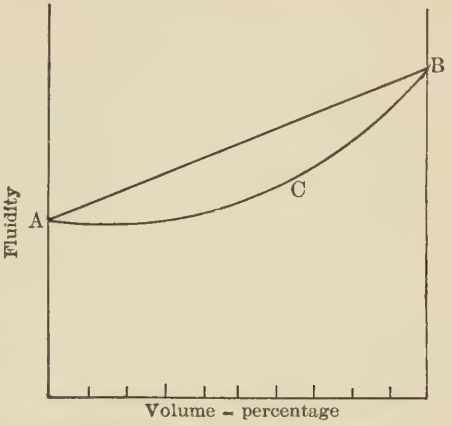


FIG. 29.—GRAPHIC REPRESENTATION OF FLUIDITY.
ACB indicates combination and *AB* does not.

Sometimes a determination of the *viscosity* of a liquid mixture indicates an association of its molecules. The viscosity is measured by determining the rate of efflux of a known volume of the liquid through a capillary. During the operation, the maintenance of a constant temperature is essential, any alteration producing a marked change in the observed value. The rate of efflux is proportional to the viscosity.

The *fluidity* (ϕ) is the reciprocal of the viscosity (η), or $\phi = \frac{1}{\eta}$. As indicated by BRIGHAM, the fluidity-curve obtained by plotting the volume-percentages of the liquid mixture as abscissæ in a co-ordinate system, and the fluidity-values as ordinates, is a straight line for many binary liquid mixtures. For mixtures such as alcohol and water, acetic acid and water, and others, instead of a straight line a curve like *ACB* (Fig. 29) is obtained, a phenomenon possibly indicative of the union of two kinds of molecules.

A fifty-five per cent. solution of glacial acetic acid in water has the same density as the pure anhydrous acid. At first, addition of water to glacial acetic acid raises the density; further addition of water causes it to fall. This circumstance makes it impossible to determine by the simple use of the hydrometer the amount of acid present in such mixtures.

The best method of ascertaining the strength of very concentrated acetic acid consists in an observation of its melting-point, a thermometer graduated in tenths of a degree being employed. In accordance with the formula given in **12**,

$$AM = \text{Constant},$$

the constant for glacial acetic acid being 39, the presence of one per cent. of water (molecular weight 18) would cause a depression (A) of $\frac{39}{18}$, or 2·16°.

A thermometer graduated in tenths being readable easily to one-twentieth of a degree, the amount of water can be determined to $\frac{1}{2 \cdot 16 \times 2}$, or 0·025 per cent., a degree of accuracy unattainable by titration.

In the absence of need for very great accuracy, and also with dilute acetic acid, the best method of determining the strength is to titrate a weighed quantity of the solution with a standard solution of alkali.

The vapour-density of acetic acid at temperatures slightly above its boiling-point is twice as great as that corresponding with the formula $C_2H_4O_2$, but near 200° it is normal. A similar phenomenon has been observed with many acids of this series and with other substances.

Absolutely pure acetic acid is not attacked by chlorine or bromine in absence of light. The acid can be prepared in this condition by distilling from phosphoric acid the highly concentrated acid melting above 16°.

83. The *acetates*, or salts of acetic acid, are soluble in water, the silver salt dissolving with difficulty. Addition of ferric chloride to a solution of an acetate such as sodium acetate produces a blood-red colour due to the formation of a complex acetoferric acetate, the salts of formic acid and of propionic acid reacting similarly. From a solution of sufficient dilution, boiling precipitates brown-red basic ferric acetate, $Fe(OH)_2C_2H_3O_2$, acetic acid being liberated simultaneously.

The dry distillation of anhydrous sodium acetate with soda-lime produces methane:

$$CH_3 \cdot COONa + NaOH = CH_4 + Na_2CO_3.$$

This method is not applicable to the salts of the higher members of this series of acids, the hydrocarbons being decomposed at the high temperature essential for the reaction.

A very delicate test for acetic acid is the formation of cacodyl oxide (**73**). The extremely poisonous nature of this substance necessitates great care in the application of the test. Among the acetates of technical importance are *lead acetate* ("sugar of lead"), *basic lead acetate*, and *aluminium acetate*. The first two are utilized in the manufacture of white lead, and the third as a mordant in calico-printing (**374**).

Butyric or Propanecarboxylic Acids, $C_4H_8O_2$.

84. Two isomeric acids with the formula $C_4H_8O_2$ are known, *normal butyric* or *propanecarboxylic*-1 *acid*, $CH_3 \cdot CH_2 \cdot CH_2 \cdot COOH$, and *iso-butyric* or *propanecarboxylic*-2 *acid*, $\frac{CH_3}{CH_3} > CH \cdot COOH$. The constitu-

tion of these acids is indicated by their synthesis, the normal compound being obtained from *n*-propyl iodide, and the *iso*-acid from *iso*propyl iodide:

$$CH_3 \cdot CH_2 \cdot CH_2I \rightarrow CH_3 \cdot CH_2 \cdot CH_2 \cdot CN \rightarrow CH_3 \cdot CH_2 \cdot CH_2 \cdot COOH.$$

$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CHI \rightarrow \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CH \cdot CN \rightarrow \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CH \cdot COOH.$$

The normal compound derives its name from the fact that it is obtainable from butter. It is also named "Fermentation butyric acid," as under certain conditions it can be produced by the fermentation of such substances as sugar, the method most suitable for its preparation. It has an extremely disagreeable odour, and can be oxidized only with difficulty.

iso*Butyric acid* also has a very disagreeable odour. It contains a tertiary carbon atom; and such compounds being oxidized readily, oxidation affords a method of distinguishing the normal acid from the *iso*-acid.

The calcium salts of these acids also exhibit a remarkable difference, that of the normal acid being less soluble in hot water than in cold, but that of the *iso*-acid following the ordinary rule and being more soluble in hot water than in cold. On being heated to approximately 80°, a solution of normal calcium butyrate saturated at 0° deposits a considerable proportion of the salt.

In accordance with the *principle of mobile equilibrium* ("Inorganic Chemistry," **236**), calcium *n*-butyrate should dissolve in water with slight evolution of heat, and calcium *iso*butyrate with slight absorption of heat. This view is supported fully by the results of experiment.

Higher Fatty or Alkanecarboxylic Acids, $C_nH_{2n}O_2$.

85. Many of the higher members of the series of fatty acids are natural products, chief among them being *palmitic* or *pentadecanecarboxylic*-1 *acid*, $C_{16}H_{32}O_2$, and *stearic* or *heptadecanecarboxylic*-1 *acid*, $C_{18}H_{36}O_2$, both with normal carbon chains (**137**). In the form of esters of glycerol (**155**), these two acids occur in large quantities as the principal constituents of most animal and vegetable fats, and are obtained from them by saponification, a process involving heating either with slaked lime (**95**), or with concentrated sulphuric acid. The mineral acid induces slight carbonization, imparting a dark colour to the fatty acids. They can be purified by distillation with superheated steam.

Another method of decomposing the fats into glycerol and a fatty acid depends on the action of an enzyme (**222**) present in castor-seed (*Ricinus*

communis). After removal of the oil, the powdered seeds are mixed intimately with the fat; on addition of a dilute acid, such as decinormal sulphuric acid, an emulsion is formed. By maintaining the mixture at a temperature between 30° and 40° for two or three days, the fatty acids are liberated in a very pure state; on gentle heating, the emulsion separates into two layers, the upper consisting of the free acids, and the lower of an aqueous solution containing between 40 and 50 per cent. of glycerol.

TWITCHELL'S process also depends on the formation of an emulsion. A mixture of the fat with water containing a few tenths of one per cent. of sulphuric acid is kept in an emulsified condition by means of live steam, the operation being rendered possible by the addition as "Saponifier" of a fatty-aromatic sulphonic acid such as naphthalenestearosulphonic acid, a substance soluble in both water and fat.

Saponification of fats yields a mixture of acids, semi-solid at the ordinary temperature. This mixture contains the two acids cited, one in the pure state melting at 62° and the other at 69°; but with a mixture of the two each lowers the melting-point of the other (25). Liquid oleic acid, belonging to another homologous series, is present also, and can be pressed from the mixture, leaving a white solid substance employed in the manufacture of "stearine" candles. For this purpose the "stearine" is melted, and after addition of a small proportion of paraffin-wax to prevent crystallization of the fatty acids, and consequent brittleness in the candles, the molten substance is poured into moulds with wicks fastened in their axes.

Soaps consist chiefly of the alkali-metal salts of the acids contained in fats. They are prepared by saponifying fats with a solution of sodium hydroxide or of potassium hydroxide heated to the boiling-temperature. Potassium-soap is termed "soft soap," and usually is yellow. In some countries it is tinted green by the addition of indigo, and then is known as "green soap." Potassium-soap contains not only the potassium salts of the acids, but also the glycerol produced in the reaction, and a considerable proportion of water. Sodium-soap is hard; after saponification is complete it is separated from the reaction-mixture by "salting-out" through addition of solid common salt to the mixture at the boiling-temperature. The sodium salts of the acids being insoluble in a concentrated solution of sodium chloride, the soap separates in the molten state, forming a layer on the surface of the brine, the glycerol remaining dissolved. The soap obtained consists of the sodium salts of the acids, with a small percentage of water.

86. In explaining the cleansing action of soap it is necessary first to indicate the causes of the soiling of the skin and clothing. It is due

partly to substances of a fatty nature, and partly to soot, iron oxide, or clay. Formerly the action of the soap was attributed to the liberation of free alkali through hydrolysis, the alkali being assumed to emulsify the fatty substances and thereby to remove the other impurities simultaneously. Later the extent of the hydrolysis was found to be very small, being of the order of $\frac{N}{1000}$. Alkali-solutions so dilute as those formed by the hydrolysis are incapable of emulsifying fats, whereas soap-solutions do emulsify them.

Modern views attribute the cleansing power of soap to its colloidal nature. The principal factors involved are indicated in the context.

1. The soap must be in solution. Sodium palmitate and sodium stearate are almost insoluble in cold water, but with such water the soluble sodium oleate constitutes an ideal washing reagent. The palmitate and stearate are very soluble in boiling water, and at its temperature are much better adapted for washing than the soaps formed from the lower alkanecarboxylic acids, these soaps being less colloidal.

2. The emulsifying power is contingent on the soap-solution having a low surface-tension. It is very remarkable how traces of soap, such as the proportion present in a solution of sodium oleate of 0·0001N strength, reduce the surface-tension of water by one-twentieth. In consequence a soap-solution is well adapted to penetrating the capillary interstices and eliminating the dirt.

3. The moistening effect of the undecomposed soap in solution.

4. The power of soap to form with impurities, such as rust, colloidal adsorption-compounds incapable of adhering to the material. By this means the impurities are removed from the fabric, and remain in stable suspension.

Soap-solutions belong to a special type of colloids named *colloid electrolytes* by Bain and Salmon. These substances are salts, and one of their ions is a very highly charged particle. For instance, the anion of sodium palmitate consists of several, say ten, palmitate ions united to constitute a single particle and carrying the same number, ten, of negative electric charges. The conductivity of such a colloidal electrolyte is wholly comparable with that of an ordinary electrolyte such as sodium acetate; because despite the diminution in mobility occasioned by the size of such an anion, there is the compensating effect of its high electrical charge. The osmotic effect of such an aggregate of ions is the same as that of a single ion, and therefore is relatively small. Consequently, the high conductivity of such compounds is associated with a small depression of the freezing-point and elevation of the boiling-point.

Water containing a certain percentage of calcium salts is termed "Hard" ("Inorganic Chemistry," 261). With soap such water does not lather immediately, but causes the formation of a white flocculent substance consisting of insoluble calcium salts of the fatty acids. Hard water is unsuitable for washing because it prevents the formation of a lather, and also because the alkali is eliminated through neutralization by the acid-radical of the calcium salts (sulphate and carbonate) present.

Electrolytic Dissociation.

87. On solution in water, molecules of acids, bases, and salts are assumed to be resolved into ions charged with opposite kinds of electricity ("Inorganic Chemistry," 65 and 66). In such a solution an acid is dissociated partially or completely into positively charged hydrogen ions, $H^{\cdot}$ (cations), and negatively charged anions, the phehomenon being exemplified by the resolution of acetic acid into $H^{\cdot}$ (positive), and $(C_2H_3O_2)'$ (negative). Bases yield a positively charged metallic ion and a negatively charged OH'-ion; salts give a positively charged metallic ion and a negatively charged acid-radical ion.

In the solution of a partly-ionized substance there is an equilibrium expressible for a monobasic acid by

$$ZH \rightleftarrows Z' + H^{\cdot},$$

Z' representing the acid-radical (*Ibid.*, 66). If v be the volume in litres containing one gramme-molecule of the acid, and α be the portion ionized, then the concentration of the ions is $\frac{\alpha}{v}$, and that of the non-ionized portion is $\frac{1-\alpha}{v}$. The equation representing the equilibrium in the foregoing example of a monobasic acid (*Ibid.*, 50) is

$$k\frac{1-\alpha}{v} = \left(\frac{\alpha}{v}\right)^2, \quad \text{or} \quad \frac{\alpha^2}{v(1-\alpha)} = k.$$

In this equation k is constant, and it is termed the *ionization-constant.* This equation has been proved to afford an exact measure of the amount of ionization for the very weak organic acids, expressing accurately the connexion between the dilution v and the ionization α. For this reason it is entitled the *law of dilution.* It was discovered by Ostwald, his procedure being to dissolve a gramme-molecule of an acid in different quantities of water v, and to ascertain the ionizations α by determining the electric conductivity. On substituting the values obtained for α

and v in the expression $\frac{\alpha^2}{v(1-\alpha)}$, it was found always to have the same value, in accord with the constancy of k.

The accuracy of this law is evident from the examples in the following table:

Acetic Acid.			Propionic Acid.			*n*-Butyric Acid.		
v	100α	10^4k	v	100α	10^4k	v	100α	10^4k
8	1·193	0·180	8	1·016	0·130	8	1·068	0·144
16	1·673	0·179	16	1·452	0·134	16	1·536	0·150
32	2·380	0·182	32	2·050	0·134	32	2·165	0·149
64	3·33	0·179	64	2·895	0·135	64	3·053	0·150
128	4·68	0·179	128	4·04	0·133	128	4·292	0·150
1024	12·66	0·177	1024	10·79	0·128	1024	11·41	0·144

88. The "strength" of acids depends on their degree of ionization, that of strong acids being considerable, and that of weak acids slight. Since the constant k rises or falls in value simultaneously with α, and is independent of the concentration, it affords a convenient measure of the strength of an acid.

The table indicates the values of 10^4k for certain fatty acids:

Formic	Acetic	Propionic	*n*-Butyric	Valeric
2·14,	0·18,	0·13,	0·15,	0·16

The ionization-constant, and consequently the strength, of formic acid are greater than those of its homologues, another example of the difference between it and the other members of the series.

A comparison of these acids with such strong mineral acids as sulphuric acid and hydrogen chloride from the point of view of the magnitude of their ionization-constants reveals the fatty acids to be very much weaker. When $v=16$, for hydrogen chloride $100\alpha=95{\cdot}55$, and for acetic acid only 1·673. Obviously 100α is the amount ionized expressed in percentage.

The weak organic acids follow the law of dilution, but the strong mineral acids do not. A perfectly satisfactory explanation of this phenomenon has not been suggested hitherto.

DERIVATIVES OF THE FATTY ACIDS OBTAINED BY MODIFYING THE CARBOXYL-GROUP.

89. The carboxyl-group can be modified by the exchange of its oxygen atoms or hydroxyl-group for other elements or groups. The compounds described in this chapter contain such modified carboxyl-groups.

I. Acid Chlorides.

Acid chlorides are derived from acids by replacement of the hydroxyl-group by chlorine, and consequently contain the group —COCl. They are obtained from the acids by the action of the chlorides of phosphorus, PCl_5 and PCl_3, or of phosphorus oxychloride, $POCl_3$:

$$3C_nH_{2n+1}\cdot COOH + 2PCl_3 = 3C_nH_{2n+1}\cdot COCl + P_2O_3 + 3HCl.$$

The ease of conversion of the acid chlorides into the corresponding acids proves the chlorine atom to have replaced the hydroxyl-group. For the lower members this conversion is effected merely by bringing them into contact with water. If the chlorine atom had substituted hydrogen of the alkyl-group, there would be no reaction, an alkyl chloride not being decomposed by water at the ordinary temperature.

The lower members of this series are liquids with a suffocating and irritating odour. The chloride corresponding with formic acid is not known. *Acetyl chloride*, CH_3COCl, fumes in the air, and can be distilled without decomposition. It boils at 55°, and at 0° its density is 1·13.

Acetyl chloride is employed in detecting the presence of hydroxyl in organic compounds. The hydroxyl-hydrogen is replaced by acetyl, the reaction being exemplified by the conversion of alcohols into esters of acetic acid:

$$R\cdot O\boxed{H+Cl}OC\cdot CH_3 = RO\cdot OC\cdot CH_3 + HCl.$$

The compound under examination is kept in contact with acetyl chloride for some time, either at the ordinary temperature or with gentle warm-

ing. The formation of an acetyl-compound is detected by analysing or saponifying the purified product, production of acetic acid by saponification proving the presence of an acetyl-derivative.

Sometimes the homologues of acetyl chloride are employed also in the detection of hydroxyl-groups.

The acid chlorides react also with the mercaptans, forming substances analogous to acetyl-compounds.

II. Acid Anhydrides.

90. *Acid anhydrides* are formed by the interaction of the alkali-metal salts of acids and acid chlorides:

$$CH_3 \cdot CO\boxed{Cl+Na}O \cdot OC \cdot CH_3 = O < \begin{matrix} OC \cdot CH_3 \\ OC \cdot CH_3 \end{matrix} + NaCl.$$

Acetic anhydride

The best method of obtaining the higher anhydrides consists in heating the sodium salts of the higher acids with acetic anhydride.

The acid chlorides can be regarded as mixed anhydrides of hydrogen chloride and an organic acid, a view supported by their formation from a mixture of these acids by the action of phosphorus pentoxide as a desiccator.

Mixed anhydrides of fatty acids only exist. Distillation decomposes them into the anhydrides of the two acids.

The lower members of this series are liquids of disagreeable, suffocating odour. *Acetic anhydride* has the density $D_4^{20} = 1 \cdot 0820$ and boils at 139·53° under a pressure of 760 mm. At the ordinary temperature it is soluble in about ten times its volume of water, the solution decomposing slowly with formation of acetic acid. In this respect it differs from acetyl chloride, which reacts momentarily and vigorously with water, yielding acetic acid and hydrochloric acid. Like acetyl chloride it is employed in testing for the presence of the hydroxyl-group. An anhydride of formic acid is not known.

III. Esters.

91. *Esters* are produced by the interaction of acid chlorides or anhydrides and alcohols:

$$CH_3 \cdot CO\boxed{Cl+H}OC_2H_5 = CH_3 \cdot COOC_2H_5 + HCl.$$

They are formed also by direct treatment of the alcohol with the acid, although extremely slowly at the ordinary temperature:

$$CH_3 \cdot COOH + HOC_2H_5 = CH_3 \cdot COOC_2H_5 + H_2O.$$

The velocity of the reaction is increased greatly by rise of temperature. Esters are obtained also by the action of the silver salt of an acid on an alkyl iodide.

A characteristic method frequently applied to the preparation of these compounds involves the passage of dry hydrogen chloride through a boiling mixture of absolute alcohol and the anhydrous organic acid. After the lapse of some time the reaction-mixture is cooled and poured into water, the ester separating owing to its slight solubility. The formation of esters in this manner can be explained by assuming a very small proportion of the hydrogen chloride to unite with the organic acid, water being eliminated, and a minute quantity of the acid chloride formed:

$$CH_3 \cdot COOH + HCl = CH_3 \cdot COCl + H_2O.$$

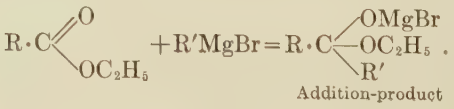
In accordance with this equation for each molecule of acid chloride generated there is produced an equivalent quantity of water, sufficient to reconvert the chloride into the organic acid and hydrogen chloride. The number of molecules of alcohol available for action on the chloride is so much larger than that of the molecules of water as to render the probability of the formation of an ester very much greater than the probability of the regeneration of the acid. The preponderance continues so long as the proportion of alcohol present greatly exceeds that of the water formed; and with the maximum yield of ester as objective the organic acid should be dissolved in a large excess of alcohol. The formation of esters is termed *esterification*.

The esters are colourless liquids of neutral reaction, and do not mix with water in all proportions. They are lighter than water, most of them having a density between 0·8 and 0·9. Many of them are characterized by their agreeable fruit-like odour, a property utilized practically in the manufacture of artificial fruit-essences. iso*Amyl* iso*valerate* (b.p. 196°) has an odour of apples, *ethyl butyrate* (b.p. 121°) of pineapples, iso*amyl acetate* (b.p. 148°) of pears, and so on.

Beeswax is a natural ester, and consists chiefly of myricyl palmitate, $C_{15}H_{31} \cdot COOC_{30}H_{61}$.

Esters can be converted into primary alcohols by reduction, effected by adding sodium to a solution of the ester in ether floating on an aqueous solution of sodium acetate, the reaction-mixture being maintained neutral by the addition of acetic acid drop by drop.

Tertiary alcohols can be synthesized from the esters by means of GRIGNARD'S alkyl magnesium halides (**75**):



Addition-product

The addition-product reacts with a second molecule of the alkyl magnesium halide:

$$R\cdot C\begin{cases}OMgBr\\OC_2H_5\\R'\end{cases} + R''MgBr = R\cdot C\begin{cases}OMgBr\\R''\\R'\end{cases} + C_2H_5OMgBr.$$

On decomposition with water the tertiary alcohol is generated:

$$R\cdot C\begin{cases}OMgBr\\R''\\R'\end{cases} + H_2O = R\cdot C\begin{cases}OH\\R''\\R'\end{cases} + MgBrOH.$$

R, R′, and R″ represent alkyl-groups.

92. The formation of esters has been investigated carefully by several chemists, initially by Berthelot and Péan de St. Gilles. Their researches demonstrated the reaction between the acid and the alcohol never to be complete, a proportion of each remaining uncombined irrespective of the duration of the process. With equivalent quantities of acetic acid and ethyl alcohol, for each gramme-molecule of alcohol and of acid present the final product contains only two-thirds of a gramme-molecule of the ester and an equivalent proportion of water, one-third of a gramme-molecule of the alcohol and a like proportion of the acid remaining uncombined. The same limit is reached through contact of equivalent quantities of an ester and water. An *equilibrium* between the four substances, alcohol, acid, ester, and water, is attained, and is a result of the *reversibility* of the reaction ("Inorganic Chemistry," 50). It may be represented by the scheme

$$C_2H_5\cdot OH + CH_3\cdot CO\cdot OH \rightleftarrows CH_3\cdot CO\cdot OC_2H_5 + H_2O.$$

The equation of equilibrium induced in *Ibid.*, 49 and 50, can be applied to the formation and decomposition of esters. It is

$$k(p-x)(q-x) = k'x^2, \quad \text{or} \quad (p-x)(q-x) = Kx^2,$$

p being the initial concentration of the alcohol and q that of the acid, and x representing the proportion of water and ester present after attainment of the equilibrium. All the quantities are expressed in gramme-molecules, and K is a constant. Two opposing reactions proceed simultaneously, all the statements cited (*loc. cit.*) being applicable. Given p, q, and K, the unknown quantity x can be calculated.

Numerous observations have proved K to equal 0·25 for the system *ethyl alcohol+acetic acid*. For contact of one gramme-molecule of alcohol

(46 g.) with one gramme-molecule of acetic acid (60 g.) both p and q are equal to 1, and the equation becomes

$$(1-x)^2=0{\cdot}25x^2, \quad \text{or} \quad x^2-\tfrac{8}{3}x+\tfrac{4}{3}=0.$$

One of the roots of this equation is $x=\frac{2}{3}$. The other root is equal to 2, but as the value of x in this reaction cannot exceed unity, this root lacks significance. The equilibrium system therefore contains $\frac{1}{3}$ *gramme-molecule of alcohol*$+\frac{1}{3}$ *gramme-molecule of acetic acid*$+\frac{2}{3}$ *gramme-molecule of water*$+\frac{2}{3}$ *gramme-molecule of ester.*

93. Several deductions established by experiment long before the development of the theory can be made from the equation

$$(p-x)(q-x)=Kx^2.$$

1. The esterfication is approximately quantitative only with a large excess of either the acid or the alcohol.

Putting the equation in the form

$$\frac{p-x}{x}=K\frac{x}{q-x},$$

obviously for an infinitely great quantity of alcohol (p) the left-hand side $=\infty$. With $q=x$ the right-hand side also is equal to ∞, all the acid having been converted into ester. This statement holds also when the ratio of the quantity of acid to alcohol is infinitely great, the whole of the alcohol changing into ester.

Although these considerations indicate esterification to be complete only in presence of an infinitely great excess of acid or alcohol, in practice a very nearly theoretical yield of ester is obtained with a finite ratio between the quantity of acid and alcohol, or between that of alcohol and acid. With 1 gramme-molecule of acetic acid and 0·05 gramme-molecule of alcohol the equilibrium corresponds with 0·049 gramme-molecule of ester, and the conversion of the alcohol into the ester is almost complete. With the gramme-molecular proportion of acetic acid and alcohol as 1 : 8, the equilibrium corresponds with 0·967 gramme-molecule of ester, and there is almost complete conversion of the acid into ester.

2. The alcohol and the acid exercise a similar influence on the formation of esters. This fact can be demonstrated by preparing a mixture containing a certain number of acid molecules and n times as many alcohol molecules, and another with the proportions of acid and alcohol reversed, the number of molecules of acid converted into ester in the first mixture being found to be equal to that of the molecules of alcohol converted in the second.

For a mixture of p gramme-molecules of alcohol and np gramme-molecules of acid, the equation becomes

$$\frac{p-x}{x}=K\frac{x}{np-x}.$$

Inversely, addition of np gramme-molecules of alcohol to p gramme-molecules of acid corresponds with

$$\frac{np-x}{x}=K\frac{x}{p-x}.$$

These equations are identical.

3. The addition of a quantity of the ester to the mixture of the alcohol and the acid at the beginning of the experiment has a similar effect on the formation of ester as adding an equivalent quantity of water.

When r gramme-molecules of water or of ester are added to a mixture containing p gramme-molecules of alcohol and q gramme-molecules of acid, the equation for both types becomes

$$(p-x)(q-x)=Kx(x+r),$$

indicating the equilibrium to be influenced to the same extent by the addition of an equivalent quantity of water or of ester.

94. A typical application of the principle of mobile equilibrium ("Inorganic Chemistry," **236**) can be made to the formation of esters. Although the velocities of formation and decomposition of esters depend greatly on the temperature, a change in it has very small effect on the equilibrium. At 10° the limit of esterification is 65·2 per cent.; at 220° it is 66·5 per cent. In accordance with the principle of mobile equilibrium, this fact indicates a very small heat of formation for the ester, a theoretical assumption established by experiment.

For the esterification of primary, secondary, and tertiary alcohols with trichloroacetic acid, $CCl_3\cdot COOH$, Michael proved the velocity-constant k to have a much higher value for primary alcohols than for the secondary and tertiary compounds. For *n*-propyl alcohol $k\times10^5=725$, for *iso*propyl alcohol 98. For secondary and tertiary alcohols the value of the constant is of the same order: for secondary butyl alcohol, $CH_3\cdot CHOH\cdot C_2H_5$, $k\times10^5=90$; for trimethylcarbinol, $(CH_3)_3C\cdot OH$, it is 118. For methyl alcohol the constant has a much higher value than for other primary alcohols, since $k\times10^5=3690$. All these determinations were made at a temperature of 25°.

In these and numerous other reactions the velocity-constant depends not only on the nature of the interacting substances, but also on various other factors, and can therefore be augmented or diminished. An example of its increase through addition of acids is given in 91, and another in 95. Moureu investigated numerous examples of negative catalysis, whereby a reaction can be decelerated by addition of a very small quantity of a substance. In connexion with the formation of esters Bailey discovered an important instance of this phenomenon, induced by adding a trace of pyridine, seven parts of this catalyst to 100,000 parts of the solution reducing the velocity of the reaction to about half its normal value.

As a necessary preliminary to reaction between two or more molecules, they must be in such very close proximity as to cause collision with one another. For gases the number and energy of such collisions can be calculated. All the molecules of a gaseous mixture or of a solution do not react simultaneously, for otherwise the velocity of reaction would be infinitely great. Originally only molecules with a velocity exceeding a certain limit were assumed to be capable of reacting with each other. This assumption appears to be untenable, because for different conditions of temperature, pressure, and concentration it is possible to calculate accurately the number of molecules with a velocity exceeding a selected limit, and their number is not proportional to the velocity-constant.

Many years ago Arrhenius suggested a hypothesis to explain the facts, and with the lapse of time it is attracting increasing attention. It postulates the necessity for the molecules to be in an *active state* as a condition of ability to interact.

95. The conversion of an ester into an acid and an alcohol by a mineral acid or an alkali is termed *saponification* from analogy to the formation of soap from alkali and fat (85). It is represented by an equation of the type

$$CH_3 \cdot COOC_2H_5 + H_2O = CH_3 \cdot COOH + C_2H_5OH,$$

the action of the mineral acid being catalytic. Its presence only accelerates the saponification, the same result being possible of attainment without it, though the time required would be incomparably longer. If the concentration of the ester be C_1, that of the water be C_2, and x be the quantity of ester saponified during the time t, the velocity of saponification $S = \frac{dx}{dt}$ for each moment can be represented by the equation for bimolecular reactions ("Inorganic Chemistry," 51):

$$S = \frac{dx}{dt} = k(C_1 - x)(C_2 - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

With a solution of an ester in a very large proportion of water the concentration C_2 of the water is altered only very slightly by the saponification, and it can be included in the constant, the equation being simplified to that for a unimolecular reaction,

$$\frac{dx}{dt} = k_1(C_1 - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The saponification of esters by bases can be represented by an equation of the type

$$CH_3 \cdot COOC_2H_5 + NaOH = CH_3 \cdot COONa + C_2H_5OH.$$

It is a bimolecular reaction, and consequently equation (1) is applicable to it.

The velocity of saponification of esters by acids depends largely on the acid, and increases with the strength of the acid. Its value has been proved to depend on the extent of electrolytic dissociation of the acid employed, indicating the saponifying action to be due to the hydrogen ion common to all acids. The velocity with bases is much greater than with acids, the ratio of the velocity-constants K for the saponification of methyl acetate by decinormal solutions of potassium hydroxide and hydrogen chloride being 1350 : 1. The velocity of saponification by bases depends also on their electrolytic dissociation, a phenomenon exemplified by ammonium hydroxide. It is ionized to a considerably less extent than potassium or sodium hydroxide, and saponifies much more slowly than either of these bases. Saponification is therefore caused by the hydroxyl-ion common to all bases.

The velocity of ester-saponification is proportional to the concentration of the hydrogen ions or hydroxyl-ions, and can be employed in determining this concentration. By its aid, the degree of hydrolytic dissociation of potassium cyanide, carbonates of alkali-metals, and other salts can be ascertained, and also the hydrogen-ionization of primary salts such as potassium hydrogen sulphate, $KHSO_4$. The non-ionized portions of the molecules are assumed not to exert any influence.

In the technical saponification of fats with slaked lime (85) a much smaller proportion of the base is employed than that needed to neutralize all the acid obtained, but the saponification is complete. This phenomenon is due to the very weak character of the higher fatty acids, their salts undergoing partial hydrolytic dissociation; and also to the fact of the very sparing solubility of these acids in water causing them to separate almost completely from that solvent. Notwithstanding the excess of acid, enough of the free base (hydroxyl-ions) to effect the saponification is present.

In addition to their decomposition by *hydrolysis*, causing the formation of an alcohol and an acid through the addition of the elements of water, the esters can undergo *alcoholysis* in accordance with such a scheme as

$$R\cdot COOCH_3+C_4H_9OH=R\cdot COOC_4H_9+CH_3OH.$$

In this reaction one alkyl-group replaces the other. The transformation can be induced at the ordinary temperature under the influence of a small proportion of an alkoxide as catalyst.

IV. Acid Amides, $C_nH_{2n+1}\cdot CONH_2$.

96. *Acid amides* are formed by the action of ammonia on acid chlorides or anhydrides, a method affording a proof of their constitution:

$$C_nH_{2n+1}\cdot CO\boxed{Cl+H}NH_2=C_nH_{2n+1}\cdot CONH_2+HCl;$$

$$\begin{matrix}C_nH_{2n+1}\cdot CO\\ C_nH_{2n+1}\cdot CO\end{matrix}>\boxed{O+\begin{matrix}H\\H\end{matrix}}\begin{matrix}NH_2\\NH_2\end{matrix}=2C_nH_{2n+1}\cdot CONH_2+H_2O.$$

Acid amides are formed also by strong heating of the ammonium salts of the fatty acids, and by distilling the sodium salts with ammonium chloride, one molecule of water being eliminated:

$$C_nH_{2n+1}\cdot CO\boxed{O}\boxed{NH_2}\boxed{H_2}=C_nH_{2n+1}\cdot CONH_2+H_2O.$$

On warming the carbonitriles with acids, two molecules of water are added, with formation of the corresponding acids (**79**). By dissolving the carbonitrile in concentrated sulphuric acid this reaction can be modified so as to limit the addition of water to one molecule, amides being obtained:

$$C_nH_{2n+1}\cdot CN+H_2O=C_nH_{2n+1}\cdot CONH_2.$$

The transformation indicates the acid amides to be intermediate products in the conversion of carbonitriles into acids. Distillation with such a dehydrator as phosphorus pentoxide converts amides into carbonitriles by elimination of water, whereas boiling with dilute acids or alkalis produces the corresponding acids by addition of the elements of water.

The action of ammonia on esters produces acid amides:

$$CH_3\cdot CO\boxed{OC_2H_5+H}NH_2=CH_3\cdot CONH_2+C_2H_5OH.$$

The acid amides are solid crystalline compounds, except the liquid *formamide*, $H\cdot CONH_2$. The lower members are soluble in water, and

in the pure state are odourless. *Acetamide*, $CH_3\cdot CONH_2$, melts at 82°, and distils at 222°. The remarkably high boiling-point of this substance is worthy of notice. Some specimens of it have a strong odour suggestive of the excrement of mice, due to slight traces of impurities.

The acid amides and the amines differ greatly in their behaviour. Unlike the bond between carbon and nitrogen in the amines, that in the $-C\begin{matrix}\diagup\!\!\!\diagup O\\ \diagdown NH_2\end{matrix}$-group of the amides is severed readily by boiling with acids or alkalis. Further, the basic properties of ammonia are weakened greatly by the exchange of one of its hydrogen atoms for an acid-radical; and although salts of acid amides do exist, they are decomposed by water. Acetamide hydrochloride, $CH_3\cdot CO\cdot NH_2,HCl$, formed by passing dry hydrogen chloride through an ethereal solution of acetamide, furnishes an example. The acid amides even possess acidic properties, an aqueous solution of acetamide dissolving mercuric oxide to form a compound with the formula $(CH_3\cdot CONH)_2Hg$.

The behaviour of the amides and amines towards nitrous acid is analogous, the corresponding acids and alcohols being produced by exchange of the amino-group for hydroxyl (65).

Amides can be converted into primary amines by a method described in 259.

97. Other derivatives obtainable from the acids by substitution in the carboxyl-group are described below.

Amino-chlorides are produced by the action of phosphorus pentachloride on the acid amides:

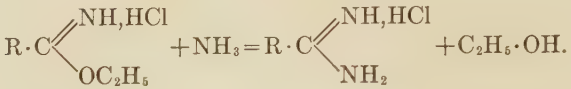
$$R\cdot CONH_2+PCl_5=R\cdot CCl_2\cdot NH_2+POCl_3.$$

Only the compounds with one or both of the hydrogen atoms of the amino-group, NH_2, replaced by alkyl are stable. The amino-chlorides yield *imino-chlorides*, $R\cdot CCl:NH$, by the elimination of one molecule of hydrogen chloride, the same compounds being formed by the addition of this chloride to carbonitriles.

Imino-ethers have the constitution $R\cdot C\begin{matrix}\diagup\!\!\!\diagup NH\\ \diagdown OR\end{matrix}$, and can be regarded as the product of the replacement of the doubly-linked oxygen of the carboxyl-group by the imino-group, NH. They are obtained by combination of alcohols and carbonitriles under the influence of dry hydrogen chloride:

$$R\cdot C\equiv N+\begin{matrix}H\\ \cdot\\ OR\end{matrix}=R\cdot C\begin{matrix}\diagup\!\!\!\diagup NH\\ \diagdown OR\end{matrix}.$$

The well-crystallized hydrochlorides of the imino-ethers are converted by ammonia into the hydrochlorides of the *amidines*:



The amidines are unstable in the free state, but are strongly monobasic, and form stable salts.

Amidoximes are addition-products of the carbonitriles and hydroxylamine, NH_2OH:

They yield salts with both acids and bases, and with an alkaline solution of a copper salt give a flocculent muddy-brown or green precipitate, a reaction affording a characteristic test for them.

Acid hydrazides are produced by the action of hydrazine, $H_2N—NH_2$, on acid chlorides or esters, indicating their constitution to be $R \cdot CONH \cdot NH_2$. Nitrous acid converts them into *acid azides*:

$$R \cdot CONH \cdot NH_2 + HNO_2 = R \cdot CON_3 + 2H_2O.$$

The acid azides are volatile explosive substances, and some yield well-developed crystals.

ALDEHYDES OR ALKANALS, AND KETONES OR ALKANONES.

98. Both the aldehydes and ketones have the general formula $C_nH_{2n}O$. They are produced by oxidation, the aldehydes from primary alcohols and the ketones from secondary alcohols. Both classes of alcohols have the general formula $C_nH_{2n+2}O$, each oxidation involving the elimination of two hydrogen atoms.

On further oxidation an aldehyde takes up one oxygen atom, forming the corresponding acid with the same number of carbon atoms, $C_nH_{2n}O$ being converted into $C_nH_{2n}O_2$. This reaction proves an aldehyde to be an intermediate product in the oxidation of a primary alcohol to an acid (45):

$$\underset{\text{Primary alcohol}}{C_nH_{2n+2}O} \rightarrow \underset{\text{Aldehyde}}{C_nH_{2n}O} \rightarrow \underset{\text{Acid}}{C_nH_{2n}O_2}.$$

A primary alcohol has the constitutional formula $C_nH_{2n+1}\cdot CH_2OH$, and on oxidation yields an acid $C_nH_{2n+1}\cdot COOH$. In this reaction the alkyl-group, C_nH_{2n+1}, is not altered, and it must be present in the aldehyde, indicating the two hydrogen atoms removed from the alcohol by oxidation to belong to the group $—CH_2OH$.

In accordance with these facts two structural formulæ are possible,

$$R\cdot C\begin{matrix}\diagup\!\!\!\diagup O \\ \diagdown H\end{matrix} \quad \text{and} \quad R\cdot C—OH.$$

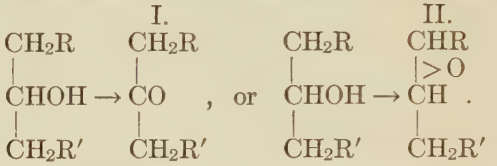
The improbability of the existence of free bonds or of bivalent carbon atoms in compounds constitutes a strong reason against the adoption of the second formula. This formula points also to the presence in an aldehyde of a hydroxyl-group, whereas the aldehydes possess none of the properties peculiar to substances containing that group. This lack is exemplified by their inability to form esters or ethers, and by the fact of phosphorus pentachloride not replacing hydroxyl by chlorine, but effecting the exchange of the oxygen atom for two chlorine atoms.

The second formula not representing the properties of the aldehydes, the first formula must be correct. This view is supported by the formation of aldehydes by the interaction of acid chlorides dissolved in moist ether and sodium, the chlorine atom being replaced by a hydrogen atom:

$$\underset{n\text{-Butyryl chloride}}{C_3H_7\cdot C\begin{matrix}\diagup Cl \\ \diagdown\!\!\!\diagdown O\end{matrix}} \rightarrow \underset{n\text{-Butyraldehyde}}{C_3H_7\cdot C\begin{matrix}\diagup H \\ \diagdown\!\!\!\diagdown O\end{matrix}}.$$

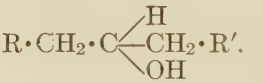
The aldehydes therefore contain the group—$C\begin{matrix}\diagup\!\!\!\diagup O \\ \diagdown H\end{matrix}$.

99. Ketones are produced by the removal by oxidation of two hydrogen atoms from secondary alcohols (45). Like the aldehydes, ketones lack the properties peculiar to hydroxyl-compounds, proving one of the hydrogen atoms to have been removed from the hydroxyl-group. Putting aside the possibility of the development of free bonds, the second hydrogen atom eliminated must have been attached to the carbon atom in union with oxygen, or to another carbon atom. The two types are represented below, R and R′ being alkyl-groups:



For reasons analogous to those for aldehydes, formula I is more probable than formula II. The products obtained by the oxidation of ketones indicate formula I to represent the constitution of this class of compounds.

The general formula for secondary alcohols is



From such an alcohol two acids, $R \cdot CH_2 \cdot COOH$ and $R' \cdot CH_2 \cdot COOH$, are obtained by strong oxidation, the carbon chain in some of the molecules being severed to the right, and in others to the left, of the CHOH-group. This reaction furnishes a means of identifying the alkyl-radicals attached to the group —CHOH— in a secondary alcohol. Since on oxidation ketones yield the same acids as the corresponding secondary alcohols, the alkyl-groups of the secondary alcohols must remain unchanged in the ketones. This fact excludes the structure represented by formula II and indicates formula I to be correct.

Ketones therefore contain the carbonyl-group —CO— *in union with two carbon atoms.*

Aldehydes can be regarded as ketones with an alkyl-group replaced by hydrogen.

Nomenclature.

The names of these compounds are formed from those of the corresponding hydrocarbons with the same number of carbon atoms by replacing the final *e* by *al* for aldehydes and by *one* for ketones.

When the term *aldehyde* is employed, the members of the aldehyde series are named after the parent acids: *formaldehyde*, $H \cdot CHO$; *acetaldehyde*, $CH_3 \cdot CHO$; *propionaldehyde*, $C_2H_5 \cdot CHO$; *valeraldehyde*, $C_4H_9 \cdot CHO$, etc. If the name *ketone* be used, the members of the ketone

series are denoted in accordance with the alkyl-groups present in them: *dimethylketone*, $CH_3 \cdot CO \cdot CH_3$; *methylpropylketone*, $CH_3 \cdot CO \cdot C_3H_7$, etc.

Methods of Formation.

100. Several methods besides the oxidation of alcohols are applicable to the preparation of both aldehydes and ketones.

1. Dry distillation of the salts of the fatty acids, calcium acetate yielding acetone:

$$\begin{matrix} CH_3 \cdot CO \\ CH_3 \cdot \end{matrix}\!\!\begin{matrix} O \\ COO \end{matrix}\!\!> Ca = CH_3 \cdot CO \cdot CH_3 + CaCO_3.$$

The conversion of acetic acid and propionic acid into the corresponding ketones is effected readily by passing the vaporized acids over aluminium oxide heated to a temperature above 400°.

Distillation of a mixture of an equivalent quantity of a formate and the salt of another fatty acid produces an aldehyde:

$$\begin{matrix} C_3H_7 \cdot CO \\ H \end{matrix}\!\!\begin{matrix} ONa \\ COONa \end{matrix} = C_3H_7 \cdot C\!\!\begin{matrix} O \\ H \end{matrix} + Na_2CO_3.$$

On distilling a mixture of the salts of two different fatty acids, excluding formates, *mixed ketones* are obtained:

$$\begin{matrix} CH_3 \cdot CO \\ C_2H_5 \cdot \end{matrix}\!\!\begin{matrix} ONa \\ COONa \end{matrix} = \underset{\text{Methylethylketone}}{CH_3 \cdot CO \cdot C_2H_5} + Na_2CO_3.$$

Ketones are formed readily by passing the free acids as vapour over precipitated aluminium oxide, Al_2O_3, at 400°.

2. Aldehydes or ketones can be obtained by heating with water compounds containing two halogen atoms attached to a single carbon atom:

$$\underset{\text{Ethylidene chloride}}{CH_3 \cdot CH\,Cl_2} + H_2O = CH_3 \cdot CHO + 2HCl.$$

3. Primary or secondary alcohols in the gaseous state passed over finely-divided copper dust, obtained by reduction of copper oxide between 250° and 400°, yield hydrogen and aldehydes or ketones:

$$C_nH_{2n+1} \cdot OH = H_2 + C_nH_{2n}O.$$

4. A useful procedure for preparing alkanals only involves bringing a carbonitrile in ether solution into contact with stannous chloride and gaseous hydrogen chloride. The reactions produce an *aldimine hydrochloride*:

$$R \cdot CN + HCl = R \cdot CCl{:}NH;$$

$$R \cdot CCl{:}NH + SnCl_2 + 2HCl = \underset{\substack{\text{Aldimine} \\ \text{hydrochloride}}}{R \cdot CH{:}NH,HCl} + SnCl_4.$$

Decomposition of the aldimine hydrochloride through the action of warm water yields the alkanal:

$$R\cdot CH{:}NH,HCl+H_2O=R\cdot CHO+NH_4Cl.$$

5. An important method for the preparation of ketones, but not of aldehydes, is the interaction of acid chlorides and zinc alkides (75), and subsequent decomposition with water. An initial addition-product is formed, its production being due to the transformation of the double bond of the oxygen atom into a single bond:

$$C_nH_{2n+1}\cdot C\begin{matrix}O\\Cl\end{matrix}+Zn\begin{matrix}CH_3\\CH_3\end{matrix}=C_nH_{2n+1}\cdot C\begin{matrix}OZnCH_3\\CH_3\\Cl\end{matrix}.$$

Water converts this addition-product into a ketone:

$$C_nH_{2n+1}\cdot C\begin{matrix}O\,|\,Zn\,|\,CH_3\quad H\,|\,O\\CH_3\qquad\qquad +\\Cl\qquad\qquad\quad H\end{matrix}=C_nH_{2n+1}\cdot CO\cdot CH_3+ZnO+CH_4+HCl.$$

101. The power of forming addition-products is common to the aldehydes and ketones. This property is due to the double bond of the oxygen atom, its conversion into a single bond liberating a carbon linking and an oxygen linking, and thus enabling the aldehydes and ketones to form addition-products with the following elements and compounds.

1. *Hydrogen.*—An addition-product is produced by the action of sodium-amalgam on an aqueous solution of an aldehyde or ketone; or by passing the vapour of the aldehyde or ketone mixed with hydrogen over heated, finely-divided nickel. Primary alcohols are formed from aldehydes, and secondary alcohols from ketones.

2. *Sodium hydrogen sulphite.*—Agitation of aldehydes or ketones with a very concentrated aqueous solution of sodium hydrogen sulphite yields a crystalline addition-product:

$$C_2H_5\cdot C\begin{matrix}O\\H\end{matrix}+NaHSO_3=C_2H_5\cdot C\begin{matrix}OH\\OSO_2Na\\H\end{matrix}.$$

This constitution is assigned to these compounds because of their ready conversion by the action of dilute acids or of sodium-carbonate solution into the corresponding aldehydes or ketones, mere solution in water effecting this change for the higher members. This reaction makes the existence of a direct bond between sulphur and carbon

highly improbable (59). Sometimes the primary sulphite compounds are termed incorrectly "bisulphite" compounds. They dissolve readily in water, but are insoluble in very concentrated solutions of the primary sulphite.

All ketones do not yield these addition-products. They are obtained most readily from those with one methyl-group in direct union with carbonyl, or methylketones.

Often primary sulphite is very serviceable for the purification of aldehydes or ketones, or for separating them from reaction-mixtures.

3. *Hydrogen cyanide.*—On contact of an aldehyde or ketone with anhydrous hydrogen cyanide and a drop of an alkaline aqueous solution of potassium carbonate, potassium cyanide, or a similar substance, combination ensues:

$$\begin{matrix}CH_3\\C_2H_5\end{matrix}>CO+HCN=\begin{matrix}CH_3\\C_2H_5\end{matrix}>C<\begin{matrix}OH\\CN\end{matrix}.$$

Addition of a small proportion of acid renders the catalyst inoperative, and the *cyanohydrins* or *hydroxycarbonitriles* formed can be obtained in the pure state by vacuum-distillation. This synthesis is important in view of the conversion of the cyanohydrins into hydroxy-acids by hydrolysis, a reaction affording a means of synthesizing such compounds (179, 5).

102. With GRIGNARD'S alkyl magnesium halides (75), aldehydes or ketones form addition-products, and with water these derivatives yield secondary or tertiary alcohols:

$$R\cdot C\begin{matrix}H\\O\end{matrix}+R'\cdot Mg\cdot I=R\cdot C\begin{matrix}H\\O\cdot Mg\cdot I\\R'\end{matrix},$$

Aldehyde — Addition-product

$$2R\cdot\overset{H}{\underset{R'}{\overset{|}{\underset{|}{C}}}}O\cdot Mg\cdot I+2H_2O=2R\cdot CHOH\cdot R'+MgI_2+Mg(OH)_2;$$

Secondary alcohol

$$\begin{matrix}CH_3\\CH_3\end{matrix}>CO+CH_3\cdot Mg\cdot Br=\begin{matrix}CH_3\\CH_3\end{matrix}>C<\begin{matrix}O\cdot Mg\cdot Br\\CH_3\end{matrix},$$

Acetone — Addition-product

$$2\begin{matrix}CH_3\\CH_3\end{matrix}>C<\begin{matrix}O\cdot Mg\cdot Br\\CH_3\end{matrix}+2H_2O=2(CH_3)_3C\cdot OH+MgBr_2+Mg(OH)_2.$$

Trimethylcarbinol

103. Other reactions characteristic of both aldehydes and ketones depend on exchange of the doubly-linked oxygen atom for other atoms or groups.

1. *Phosphorus pentachloride* replaces the oxygen atom by two chlorine atoms.

2. *Hydroxylamine* reacts in accordance with the equation

$$\begin{matrix}CH_3\\CH_3\end{matrix}>C\boxed{O+H_2}NOH=\begin{matrix}CH_3\\CH_3\end{matrix}>C{:}NOH+H_2O,$$

oximes being produced. Those from aldehydes are termed *aldoximes* and those from ketones *ketoximes*. This reaction is of very general application. The oximes are either crystalline solids or liquids, and possess both acidic and basic properties. Bases replace the hydrogen of the hydroxyl-group by a metal; acids form addition-products, the reaction being similar to the production of ammonium salts:

$$(CH_3)_2{=}NOH,HCl.$$
Acetoxime hydrochloride

On boiling with dilute hydrochloric acid, the oximes take up one molecule of water, yielding hydroxylamine and either an aldehyde or a ketone.

The constitution of the oximes is discussed in **237**.

Energetic reduction converts the oximes into amines:

$$R_2C{=}NOH+4H=R_2\underset{\dot{H}}{C}NH_2+H_2O.$$

The aldoximes are transformed readily into the corresponding carbonitriles by the action of dehydrators such as acetic anhydride.

$$C_nH_{2n+1}\cdot\underset{\boxed{H}}{C}{=}N\boxed{OH}\rightarrow C_nH_{2n+1}\cdot C{\equiv}N.$$

Ketoximes undergo a remarkable rearrangement of the atoms in the molecule or *intramolecular transformation*, named after its discoverer the "Beckmann transformation." It is induced by an agent such as acetyl chloride, the ketoximes yielding acid amides with substituents in union with the nitrogen atom:

$$\underset{\underset{NOH}{\|}}{R\cdot C\cdot R'}\rightarrow R\cdot CO\cdot NHR'.$$
Oxime Amide

The behaviour of aldehydes and ketones with *phenylhydrazine*, $C_6H_5NH\cdot NH_2$ (**310**), is exactly analogous to that with hydroxylamine:

$$\begin{matrix}R\\R'\end{matrix}>C\boxed{O+H_2}N\cdot NH\cdot C_6H_5=\begin{matrix}R\\R'\end{matrix}>C{=}N\cdot NH\cdot C_6H_5+H_2O.$$
Phenylhydrazine Phenylhydrazone

The substances formed are termed *hydrazones*, and are either well-

defined crystalline compounds or liquids. Heating with hydrochloric acid causes addition of the elements of water, with formation of phenylhydrazine and the corresponding aldehyde or ketone. Phenylhydrazine and hydroxylamine are important reagents for detecting the presence of the carbonyl-group.

The constitution of the phenylhydrazones is established by the action on aldehydes and ketones of the alkylphenylhydrazines. These derivatives of phenylhydrazine are obtained by replacement of the hydrogen of the imino-group, —NH, by an alkyl-group, and exert an action on aldehydes and ketones similar to that of phenylhydrazine itself, indicating exclusion of the structure $R_2C\left\langle\begin{matrix}NH\\ \cdot\\ N\cdot C_6H_5\end{matrix}\right.$. Confirmatory evidence is furnished by the inability of phenylhydrazines lacking an unsubstituted amino-group to form hydrazones.

ALDEHYDES OR ALKANALS.

104. Most of the aldehydes are liquids of characteristic, disagreeable odour, the lower members of the series being miscible with water in all proportions. They boil at temperatures appreciably lower than the corresponding alcohols. *Ethanal* or *acetaldehyde*, C_2H_4O, boils at 22°; ethanol, C_2H_6O, boils at 78°.

In addition to the properties common to both aldehydes and ketones (**101–103**), aldehydes have their own special properties.

1. *Aldehydeammonia.*—Acetaldehydeammonia is produced from ammonia and acetaldehyde:

$$\underset{\text{Acetaldehyde}}{C_2H_4O}+NH_3=\underset{\text{Acetaldehydeammonia}}{C_2H_4ONH_3}.$$

It is precipitated in the form of white crystals by the slow introduction of acetaldehyde into liquefied anhydrous ammonia, or by gradual addition of a concentrated aqueous solution of ammonia to the aldehyde at low temperature. It is very soluble in water, and melts at 96°–98°. Acids decompose the aldehydeammonias into an aldehyde and ammonia; potassium hydroxide is unable to effect this decomposition.

At the ordinary temperature the molecular formula of acetaldehydeammonia is three times its empirical formula. By drying over sulphuric acid it loses water, becoming transformed into a substance of the formula $(CH_3\cdot CHNH)_3$, (**105**) a polymeride of ethylideneimine. Water reconverts this product into acetaldehydeammonia.

2. *Acetals.*—An aldehyde combines with two molecules of an alcohol with elimination of water and production of an *acetal* or *dialkoxyalkane:*

$$CH_3\cdot C\begin{matrix}H\\ \boxed{O}\end{matrix}+\begin{matrix}H\\ H\end{matrix}\begin{matrix}OC_2H_5\\ OC_2H_5\end{matrix}\rightleftarrows CH_3\cdot CH<\begin{matrix}OC_2H_5\\ OC_2H_5\end{matrix}+H_2O.$$

Acetals are obtained readily by addition of the aldehyde to a one per cent. solution of anhydrous hydrogen chloride in the alcohol. As water acts on acetal, regenerating aldehyde and alcohol, the reaction is not complete, being limited by the reverse transformation. Both the formation and decomposition of acetal are accelerated considerably by the powerful catalytic influence of a small proportion of a strong mineral acid. The acetals are liquids of aromatic odour, and distil without decomposition. They are not attacked by alkalis, but are resolved by acids into the parent compounds. This fact supports the indirect union through oxygen of the alkyl-groups and the aldehyde-residue expressed in the structural formula, the stability of a carbon chain being sufficient to resist the action of such reagents.

3. *Reaction with acid anhydrides.*—Addition-products are obtained with acid anhydrides:

$$CH_3 \cdot C\overset{H}{\underset{O}{<}} + \underset{\text{Acetic anhydride}}{O(COCH_3)_2} = CH_3 \cdot CH < \begin{matrix} OCOCH_3 \\ OCOCH_3 \end{matrix}.$$

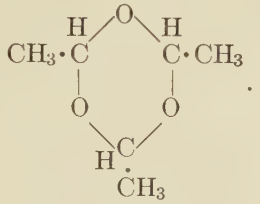
These compounds are analogous to the acetals. They are decomposed easily into the corresponding acid and aldehyde by water, and still more readily by alkalis.

105. Two types of addition-products are formed by the union of aldehyde molecules. Addition of a few drops of concentrated sulphuric acid to acetaldehyde, a liquid boiling at 22°, causes the mixture to become warm, and then to boil violently. At the end of the reaction a colourless liquid resembling the original fluid is obtained, but it boils at 124°, about 100° higher. The empirical formula of this compound is the same as that of acetaldehyde, C_2H_4O, but its vapour-density is three times as great, indicating its molecular formula to be $C_6H_{12}O_3$. This substance, *paracetaldehyde*, is converted readily into acetaldehyde by distillation with dilute sulphuric acid, another example of a reaction limited by the reverse transformation:

$$C_6H_{12}O_3 \rightleftarrows 3C_2H_4O.$$

The final equilibrium must be independent of the nature of the acid catalyst ("Inorganic Chemistry," **50,**) as has been proved for this reaction by experiment. The same equilibrium must be attained without the aid of any catalyst, but the change proceeds so slowly as to render experimental proof impossible. A direct union between the carbon atoms of the three aldehyde molecules in paracetaldehyde is improbable, and the existence of an indirect linking through the oxygen atoms must be assumed, as accounting for the ease of resolution of the

molecule of paracetaldehyde. The compound is not attacked by sodium, indicating the lack of hydroxyl-groups. It has not any of the characteristics of aldehydes, proving the absence of the group $-C\begin{matrix}O\\H\end{matrix}$. These properties are expressed by the constitutional formula



The union of two or more molecules of a substance to form a derivative capable of reconversion into the original compound is termed *polymerization.*

106. Under the influence of dilute alkali-solutions aldehyde molecules combine with production of compounds of a different type. An aqueous solution of acetaldehyde warmed with concentrated potassium hydroxide becomes yellow, and after a short time reddish-yellow amorphous masses are precipitated. The aldehyde has *resinified,* and the reddish-yellow substance formed is named *aldehyde-resin.* Addition of dilute potassium hydroxide (or sodium acetate, zinc chloride, etc.) to acetaldehyde yields a substance with the same empirical composition as acetaldehyde, but with double the molecular formula, $C_4H_8O_2$. This compound is *aldol,* a liquid capable of distillation without decomposition under diminished pressure, and readily polymerized. It possesses the properties characteristic of aldehydes, exemplified by its oxidation to an acid with the same number of carbon atoms. This acid has the formula $C_4H_8O_3$, and is a *n*-hydroxybutyric acid, or *n*-butyric acid with one hydrogen atom of the alkyl-group replaced by hydroxyl. It can be converted into *n*-butyric acid, with a chain of four carbon atoms, proving the presence of a similar chain in aldol. Obviously the formation of aldol involves the union of the aldehyde molecules through the carbon bonds, a view supported by failure to reconvert aldol into acetaldehyde. The combination of the aldehyde molecules to form aldol can be represented by the equation

$$CH_3\cdot C\begin{matrix}H\\O\end{matrix} + HCH_2\cdot C\begin{matrix}H\\O\end{matrix} = CH_3\cdot C\begin{matrix}H\\CH_2\cdot C\begin{matrix}H\\O\end{matrix}\\OH\end{matrix}$$

Aldol

This constitutional formula expresses the properties of aldol.

Instead of explaining the formation of aldol by assuming the combination of one of the hydrogen atoms of one aldehyde molecule with the oxygen atom of another to form hydroxyl, an aldehyde molecule might be supposed to unite with a molecule of water, the addition-product formed reacting with a second molecule of aldehyde with elimination of water:

$$CH_3\cdot C\begin{matrix}H\\O\end{matrix}+H_2O=CH_3\cdot \overset{H}{\overset{\cdot}{C}}<\begin{matrix}OH\\OH\end{matrix};$$

$$CH_3\cdot \overset{H}{\overset{\cdot}{C}}<\begin{matrix}OH\\ \boxed{OH+H}\end{matrix}\ CH_2\cdot CHO=CH_3\cdot \overset{H}{\overset{\cdot}{C}}<\begin{matrix}OH\\CH_2\cdot CHO\end{matrix}+H_2O.$$

Aldol

Often reactions are explained by assuming the formation of such addition-products and the subsequent elimination of water. In a few instances this assumption has been verified experimentally.

Aldol is both an alcohol and an aldehyde, hence its name, *ald*(ehyde-alcoh)*ol*. The union of molecules through carbon bonds as in the formation of aldol, with the production of compounds not reconvertible by any simple method into the original substance, is termed *condensation*.

Probably aldehyde-resin is a product of the continued condensation of the aldol molecules with elimination of water, just as under the influence of heat aldol itself loses one molecule of water readily, with formation of crotonaldehyde (142):

$$\underset{\text{Aldol}}{CH_3\cdot CHOH\cdot CH_2\cdot C\begin{matrix}H\\O\end{matrix}}-H_2O=\underset{\text{Crotonaldehyde}}{CH_3\cdot CH:CH\cdot C\begin{matrix}H\\O\end{matrix}}.$$

The mechanism of the condensation of the higher aldehydes always involves transposition of a hydrogen atom in union with the carbon atom carrying the aldehyde-group of one molecule, this hydrogen combining with the carbonyl-oxygen of another molecule to form hydroxyl, the liberated carbon valencies becoming saturated simultaneously:

$$C_nH_{2n+1}\cdot \underset{\underset{C\begin{matrix}H\\O\end{matrix}}{|}}{CHH}\xrightarrow{+}\begin{matrix}H\\O\end{matrix}C\cdot C_mH_{2m+1}=C_nH_{2n+1}\cdot \underset{\underset{C\begin{matrix}H\\O\end{matrix}}{|}}{CH}\cdot CHOH\cdot C_mH_{2m+1}.$$

Wieland made some interesting experiments on the *oxidation of aldehydes* to acids. The old theory assumed the direct union of the aldehyde with an atom of oxygen:

$$R\cdot CHO+O=R\cdot COOH.$$

WIELAND proved the mechanism of acid formation to depend on an initial combination of the aldehyde with water, the addition-product formed subsequently losing hydrogen through oxidation to water:

$$R\cdot CHO + H_2O = R\cdot CH(OH)_2;$$
$$R\cdot CH(OH)_2 = R\cdot COOH + 2H\cdot$$
$$2H + O = H_2O.$$

Agitation of an aqueous solution of aldehyde with palladium-black in absence of air produces the corresponding acid and palladium hydride. On access of air or on addition of an oxidizer, the hydrogen attached to the metal becomes oxidized, and there is a further formation of acid. The presence of water is essential to the production of acid, for although anhydrous acetaldehyde and dry silver oxide do not react, addition of water instantly induces energetic oxidation.

By means of analogous experiments, WIELAND demonstrated the conversion of primary alcohols into aldehydes to be dependent on the abstraction of two hydrogen atoms from the CH_2OH-group.

Tests for Aldehydes.

107. The following tests serve for the detection of aldehydes.

1. Resinification with alkalis.

2. Reduction of an ammoniacal silver solution. This solution is prepared by adding excess of potassium hydroxide to a solution of silver nitrate, and then exactly sufficient ammonia to dissolve the precipitated silver oxide. Warming this liquid with a dilute aqueous solution of an aldehyde is attended by the deposit on the sides of the tube of a beautiful mirror of metallic silver.

3. Addition of an aldehyde to SCHIFF's reagent, a solution of magenta (**373**) decolorized by sulphurous acid, restores the colour.

Formaldehyde or Methanal, $H\cdot C\begin{smallmatrix}\diagup O\\ \diagdown H\end{smallmatrix}$.

108. Formic acid is the first member of the homologous series of fatty acids, and it has certain properties not possessed by the higher members (**81**). *Formaldehyde* affords another striking example of this phenomenon of disparity between the first and succeeding members of a homologous series.

It is obtained by the oxidation of methyl alcohol, effected by passing a mixture of air and the alcohol-vapour over a hot spiral of platinum or copper. The heat produced by the reaction suffices to raise the

temperature of the spiral to redness, and to maintain it at that point, provided the stream of gas is passed over it with sufficient velocity. In view of its ready solubility in water, the formaldehyde produced is absorbed by that solvent.

This aldehyde is a product of the incomplete combustion of wood, of peat, and of many other organic substances. This fact explains its presence in traces in the atmosphere, especially in that of large towns. Its formation from methane and ozone is also noteworthy.

Formaldehyde has a very pungent odour. At the ordinary temperature it is gaseous, but cooling with solid carbon dioxide and ether yields a liquid boiling at $-20°$. Even at this temperature polymerization begins, and at higher temperatures it proceeds with explosive energy. Evaporation of the aqueous solution produces *paraformaldehyde*, a crystalline polymeride melting at 63°, and of unknown molecular weight. On concentrating a solution of formaldehyde with strong sulphuric acid, only part of the formaldehyde is evolved as gas, the rest polymerizing to a white crystalline mixture of α-, β-, and γ-*polyoxymethylene*. The molecular weights of these polymerides are not known. Their reconversion by heat into formaldehyde proves them to be true polymerides. Prolonged heating of the γ-variety with water yields another polymeride, δ-*polyoxymethylene*. With ammonia at the ordinary temperature formaldehyde does not give an aldehydeammonia, but the complex compound *hexamethylenetetramine*, $(CH_2)_6N_4$. It is a crystalline and very hygroscopic basic substance, and is employed as a medicine under the name "Urotropine." Between 120° and 160° and at increased pressure, methylamines are formed:

$$2NH_3+3CH_2O=2NH_2\cdot CH_3+CO_2+H_2O;$$

$$2NH_3+6CH_2O=2NH(CH_3)_2+2CO_2+2H_2O;$$

$$2NH_3+9CH_2O=2N(CH_3)_3+3CO_2+3H_2O.$$

With potassium hydroxide formaldehyde does not resinify, but is converted into methyl alcohol and potassium formate:

$$2CH_2O+KOH=CH_3OH+HCOOK.$$

This transformation is named Cannizzaro's *reaction* after its discoverer. It is of great importance in many biological processes (221).

The oxime of formaldehyde also polymerizes readily. Formaldehyde and its derivatives display a much greater tendency towards polymerization than the other aldehydes and their derivatives, and differ from them in their behaviour with ammonia and with potassium hydroxide.

An aqueous solution containing forty per cent. of formaldehyde is the commercial product "Formalin." After dilution, it is employed as a disinfectant and in the preservation of anatomical specimens. It possesses the remarkable property of converting protein substances into a hard elastic mass quite insoluble in water. The contents of a hen's egg undergo this transformation through contact with formalin for half-an-hour; brain-substance attains the consistency of india-rubber; and a solution of gelatin is converted into a hard, transparent, insoluble, odourless mass, reducible to a fine powder. Before development, photographic films with a basis of gelatin are immersed in a dilute solution of formaldehyde for a short time to render the gelatin insoluble.

The condensation of formaldehyde is discussed in **206**.

An addition-product of formaldehyde and sodium sulphoxylate, $NaHSO_2$, with the formula $CH_2O \cdot NaHSO_2, 2H_2O$, is obtained by boiling a solution of the primary sulphite compound of formaldehyde with zinc-dust. Under the name "Rongalite" it finds technical application in the reduction of vat-dyestuffs (**405**).

The concentration of a formalin solution is determined by adding excess of a solution of twice normal sodium hydroxide, and then hydrogen peroxide, the aldehyde being converted completely into formic acid. The excess of alkali is estimated by titration, and from the result the amount of formaldehyde can be calculated, one molecule of the aldehyde yielding one molecule of the acid.

Acetaldehyde or Ethanal, $CH_3 \cdot C\langle^{H}_{O}$.

109. *Acetaldehyde* is the typical aldehyde of this series, having all the properties characteristic of aldehydes as a class. It is obtained by the oxidation of ethyl alcohol by means of potassium dichromate and sulphuric acid, and is a liquid boiling at 22°, and solidifying at $-120 \cdot 6°$. In the dilute state it has a disagreeable odour. It polymerizes readily to paracetaldehyde, $C_6H_{12}O_3$ (**105**), or to *metacetaldehyde*. The molecular weight of metacetaldehyde is not known with certainty, but cryoscopic determinations point to the formula $(C_2H_4O)_4$, or to a polymeric multiple of it. Metacetaldehyde forms well-developed acicular crystals,

and begins to sublime at 150°. Neither it nor paracetaldehyde exhibits the aldehyde reactions, a characteristic exemplified by the inability of alkalis to resinify them.

The inter-relationship of acetaldehyde, paracetaldehyde, and metacetaldehyde is still a matter of doubt, but certain facts have been established definitely. Acetaldehyde is converted into paracetaldehyde by the action of various catalysts, among them sulphuric acid at ordinary or somewhat raised temperature, metacetaldehyde also being produced in small proportion. Good cooling of the liquid immediately after addition of the catalyst yields as the main product well-developed needles of metacetaldehyde, but paracetaldehyde is formed also. Under the influence of the catalyst rise of temperature decomposes the metacetaldehyde with production of acetaldehyde and paracetaldehyde. No direct transformation of metacetaldehyde into paracetaldehyde has been observed, the mechanism of the transformation probably involving a preliminary complete depolymerization to acetaldehyde, followed by the formation of paracetaldehyde.

Addition of a very small proportion of sulphuric acid to ice-cold acetaldehyde generates metacetaldehyde, converted by further addition of sulphuric acid into paracetaldehyde. Calcium chloride, a much less energetic catalyst, also induces the formation of metacetaldehyde, paracetaldehyde being produced only in traces. These facts indicate the equilibrium between acetaldehyde and metacetaldehyde to be attained much more readily than that between acetaldehyde and paracetaldehyde. The predominance of paracetaldehyde or metacetaldehyde in the ternary system

$$\text{Paracetaldehyde} \rightleftarrows \text{Acetaldehyde} \rightleftarrows \text{Metacetaldehyde}$$

is dependent on the experimental conditions, temperature being a very important factor.

In practice acetaldehyde is transformed into paracetaldehyde by addition of sulphuric acid, the catalyst being rendered inoperative by neutralization of the acid after completion of the reaction. The acetaldehyde and paracetaldehyde can be separated readily by distillation. Inversely, the conversion of paracetaldehyde into acetaldehyde is effected by addition of sulphuric acid, and distillation of the mixture from a water-bath. The volatilization of the acetaldehyde upsets the equilibrium, causing the catalyst to decompose a fresh portion of paracetaldehyde. The acetaldehyde produced distils, and the process continues until the conversion into acetaldehyde is complete.

In preparing metacetaldehyde, the acetaldehyde is cooled to a low temperature, and dilute sulphuric acid is added. Metacetaldehyde crystallizes, and can be isolated by filtration. The mode of reconverting it into acetaldehyde is similar to that described for paracetaldehyde.

KETONES OR ALKANONES.

110. The properties characteristic of the ketones are described in **101–103**. The first member of the homologous series cannot contain less than three carbon atoms.

Ketones have the general formula $R \cdot CO \cdot R'$, and by oxidation are divided always at the carbonyl-group (**99**), oxidation occurring at that part of the molecule already containing oxygen (**45**). The fission can take place in two different ways:

$$R \cdot \underset{\text{I}}{|}CO \cdot R' \quad \text{or} \quad R \cdot CO \cdot \underset{\text{II}}{|}R'.$$

Methylnonylketone, $CH_3 \cdot \underset{\text{I}}{|}CO \cdot \underset{\text{II}}{|}C_9H_{19}$, can yield formic acid, CH_2O_2, and capric acid, $C_{10}H_{20}O_2$; or acetic acid, $C_2H_4O_2$, and pelargonic acid, $C_9H_{18}O_2$; the fission occurring at the point indicated by line I or at that denoted by line II. The oxidation is such as to induce decomposition at both points simultaneously, four acids being obtained. Two of them may be identical, as in the oxidation of methylethylketone, $CH_3 \cdot CO \cdot C_2H_5$, to acetic acid and acetic acid by fission at II, and formic acid and propionic acid by fission at I. Usually the reaction leaving the carbonyl in union with the smaller alkyl-residue predominates. In this manner oxidation affords a means of determining the position of the carbonyl-group in the ketone molecule.

The ketones are distinguished from the aldehydes also by their behaviour towards ammonia, this reaction having been investigated carefully for acetone, the first member of the series. By elimination of water it yields complex substances such as *diacetoneamine*, $C_6H_{13}NO$ or $(2C_3H_6O + NH_3 - H_2O)$, and *triacetoneamine*,

$$C_9H_{17}NO \quad \text{or} \quad (3C_3H_6O + NH_3 - 2H_2O).$$

The ketones do not polymerize, but are capable of forming condensation-products.

Acetone or Propanone, $CH_3 \cdot CO \cdot CH_3$.

111. On the manufacturing scale acetone is prepared by two methods:

1. By the dry distillation of calcium acetate, or by passing the vapour of acetic acid through a tube containing a mixture of lime and magnesia heated at 485°.

2. By the yeasting of potato-starch or of other carbohydrates with a special kind of yeast, butyl alcohol being formed simultaneously (**46**).

Acetone is present in normal urine in very small proportion, but in much greater proportion in pathological cases such as *Diabetes mellitus* and *Acetonuria*. It is a liquid of peculiar peppermint-like odour, boils at 56·3°, solidifies at −93·9°, and at 0° has the density 0·812. It is an excellent solvent for many organic compounds, and is miscible in all proportions with water, addition of salts such as potassium carbonate causing the liquid to separate into two layers. By reduction it is converted into *iso*propyl alcohol (**150**), and it yields a crystalline oxime melting at 69°. Condensation-products derived from acetone are considered in **143** and **282**.

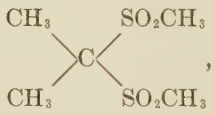
Sulphonal is an important soporific, and is prepared from acetone. In presence of hydrogen chloride, acetone unites with ethylmercaptan with elimination of water:

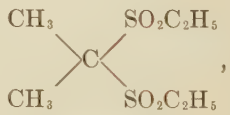
$$(CH_3)_2CO+2HS\cdot C_2H_5=(CH_3)_2C(SC_2H_5)_2+H_2O.$$

Dimethyldiethyl-mercaptole

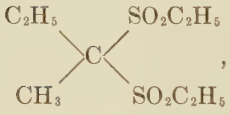
Oxidation with potassium permanganate converts the two sulphur atoms of this compound into sulphone-groups, forming diethylsulphonedimethylmethane, $(CH_3)_2C(SO_2C_2H_5)_2$, or sulphonal. It crystallizes in colourless prisms, soluble with difficulty in cold water, and melting at 126°.

The soporific action of sulphonal must be ascribed to its ethyl-groups. *Dimethylsulphonedimethylmethane* (I) lacks this property; but as its methyl-groups are replaced by ethyl-groups, the hypnotic power becomes augmented, attaining its maximum in *tetronal* (IV):

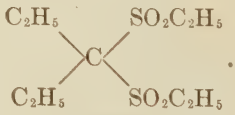
I. 

II. 

Sulphonal

III. 

Trional

IV. 

Tetronal

UNSATURATED HYDROCARBONS.

I. ALKENES OR ALKYLENES, C_nH_{2n}.

Methods of Formation.

112. The *alkenes* are formed in the dry distillation of complex carbon compounds, a fact accounting for their presence in coal-gas to the extent of four to five per cent.

2. They are produced by elimination of the elements of water from the alcohols $C_nH_{2n+2}O$:

$$C_5H_{11}\cdot OH = C_5H_{10} + H_2O.$$

Sometimes this transformation can be effected by heat alone, as with tertiary alcohols, but usually it is necessary to warm the alcohol with a dehydrator such as concentrated sulphuric acid (54 and 115) or zinc chloride. Water is eliminated more readily from the secondary and tertiary alcohols than from the corresponding primary compounds.

3. They can be obtained by abstraction of hydrogen halide from alkyl halides, effected by heating with alcoholic potash, a solution of potassium hydroxide in ethyl alcohol:

$$C_nH_{2n+1}I + KOC_2H_5 = C_nH_{2n} + KI + C_2H_5OH.$$

An ether is formed also (55):

$$C_nH_{2n+1}I + KOC_2H_5 = C_nH_{2n+1}OC_2H_5 + KI.$$

With alkyl iodides the main reaction follows the first equation, the secondary and tertiary iodides being adapted specially for the production of unsaturated hydrocarbons.

The names of the members of this series are derived from those of the saturated hydrocarbons by altering the termination "ane" to "ene"

or "ylene." These compounds are denoted by the general name *alkenes* or *alkylenes*.

Name.	Formula.	Boiling-point.	Name.	Formula.	Boiling-point.
Ethene.....	C_2H_4	−103°	*n*-Heptene.....	C_7H_{14}	98°
Propene.....	C_3H_6	− 48°	*n*-Octene.....	C_8H_{16}	124°
n-Butene.....	C_4H_8	− 5°	*n*-Nonene.....	C_9H_{18}	153°
n-Pentene.....	C_5H_{10}	39°	*n*-Decene.....	$C_{10}H_{20}$	170°
n-Hexene.....	C_6H_{12}	68°	*n*-Undecene....	$C_{11}H_{22}$	195°

The position of the double bond in the molecule is indicated by the identification-number of the first carbon atom attached to it. The formula $CH_3 \cdot CH{:}CH \cdot CH_3$ represents *butene*-2, and $(CH_3)_2C{:}CH_2$ corresponds with *methyl*-2-*propene*-1.

Properties.

113. The lower members of this homologous series are gases, and are slightly soluble in water; the higher members are liquids or solids insoluble in water, but soluble in alcohol and ether. At their melting-points the densities of the lower members are about 0·63, rising with increase in the number of carbon atoms to 0·79 approximately. They are only slightly higher than those of the corresponding saturated hydrocarbons, but their refractions are much greater (**120**). Like the saturated hydrocarbons, the alkenes are colourless.

Their most important chemical property is the power of forming addition-products, and on account of it they are said to be *unsaturated*. Addition-products are obtained very readily by the action of the halogens, especially bromine, on the alkenes and other substances containing a double bond, a structure identified by the decolorization of bromine-water. Another test for the presence of a double bond, suggested by von Baeyer, involves agitation of the substance with a dilute solution of potassium permanganate and sodium carbonate. Owing to the reducing action of compounds containing a double carbon bond, the violet colour of the permanganate quickly disappears, with formation of a brown-red flocculent precipitate of hydrated manganese dioxide. Compounds of other classes, such as aldehydes, react similarly with potassium permanganate, the test being applicable only in their absence to hydrocarbons, unsaturated acids, and a few other substances.

Of the hydrogen halides, hydrogen iodide reacts most readily with the alkenes; but, in presence of bismuth chloride or bromide, gaseous

hydrogen chloride and bromide are absorbed rapidly. Alkyl halides are formed in these reactions.

The hydrogen halides react with the alkenes by addition to form the alkyl halides, hydrogen iodide combining very readily.

Remarkable phenomena were discovered by Norris in connexion with the interaction of ethene and chlorine or bromine in the gaseous state. When a dry mixture of ethene and gaseous chlorine diluted with air is passed through a glass tube at 0°, addition takes place with measurable velocity. The proportion of dichloroethane formed can be ascertained through pressure measurements, for the pressure of the gaseous mixture diminishes as the reaction proceeds. The value of the velocity-constant determined for a bimolecular reaction depends on the cross-section of the glass tube, and is greater for a narrow tube than for a wide one. This phenomenon can be explained by assuming the reaction to take place on the glass wall of the tube and not in the open space within it. There are many examples of acceleration of reactivity between gaseous substances induced by the tube wall. For ethene and chlorine the nature of the solid wall enclosing the reacting gases can be demonstrated to influence the velocity of the reaction. In a glass tube having its inner surface carefully coated with a layer of paraffin-wax, the velocity is twelve hundred times smaller than in an uncoated glass tube; but if the surface be covered with a layer of stearic acid, the velocity-constant is of the same order of magnitude as with an uncoated glass tube. There appears to be a catalytic effect exerted by the inner surface of the reaction vessel.

Concentrated sulphuric acid yields the alkylsulphuric acids by addition, it being necessary sometimes to employ the fuming acid. The addition of sulphuric acid, like that of the hydrogen halides, induces union of the acid-residue with the unsaturated carbon atom attached to the smallest amount of hydrogen. An example is the conversion of *iso*butene, $\begin{matrix}CH_3\\CH_3\end{matrix}>C:CH_2$, by sulphuric acid or hydrogen iodide into

$$\begin{matrix}CH_3\\CH_3\end{matrix}>\underset{\displaystyle OSO_3H}{\overset{\displaystyle |}{C}}—CH_3 \quad \text{or} \quad \begin{matrix}CH_3\\CH_3\end{matrix}>\underset{\displaystyle I}{\overset{\displaystyle |}{C}}—CH_3 .$$

Normally in such addition-reactions there is a tendency for the number of methyl-groups to increase.

Hypochlorous acid, Cl·OH, also can give addition-products termed *chloro-alcohols*:

$$\underset{\text{Ethene}}{CH_2{=}CH_2}+Cl\cdot OH=\underset{\text{2-Chloroethanol}}{CH_2Cl\cdot CH_2OH}.$$

114. Alkenes can form condensation-products, butene and the pentenes yielding them under the influence of moderately dilute sulphuric acid, although ethene cannot be condensed similarly. The condensation may be explained by assuming an initial addition-product with sulphuric acid or alkylsulphuric acid to be formed, and to react with a second molecule of the alkene:

$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!C{:}CH_2 \rightarrow \begin{matrix} (CH_3)_2C\text{—}CH_3 \\ | \\ \boxed{OSO_3H+H}\,HC{:}C(CH_3)_2 \end{matrix} ; \rightarrow$$

$$\rightarrow \begin{matrix} (CH_3)_2C\text{—}CH_3 \\ | \\ HC{=}C(CH_3)_2 \end{matrix} .$$

The simplest member of this series would be *methene* or *methylene*, CH_2, but it has not been isolated. Various attempts to prepare it have been made, one method being by the elimination of hydrogen chloride from methyl chloride. Such experiments have resulted always in the formation of ethene instead of methene, two methene-groups uniting to form a single molecule.

Ethene or Ethylene, C_2H_4.

115. Ethene is a gas, and usually is prepared by heating a mixture of ethyl alcohol and sulphuric acid. Ethylsulphuric acid is the initial product (**54**), and on further heating decomposes into ethene and sulphuric acid:

$$C_2H_5SO_4H = C_2H_4 + H_2SO_4.$$

It is desirable to add as a catalyst five grammes of anhydrous aluminium sulphate per 100 c.c. of liquid. In the preparation of ether (**56**) the temperature is maintained below a certain limit, and fresh alcohol is added continually, but in this reaction a higher temperature is employed, and no alcohol is added. At the temperature of the reaction, sulphur dioxide and carbon dioxide are produced, but can be removed from the ethene by passing it through dilute alkali.

Newth's method consists in adding ethyl alcohol drop by drop to phosphoric acid heated to 200°, and yields a purer product.

Ethene can be prepared also from ethene bromide, $C_2H_4Br_2$, by removal of its two bromine atoms, effected by bringing it into contact with Gladstone and Tribe's copper-zinc couple.

Ethene possesses a peculiar sweetish odour, and burns with a luminous flame. The gas can be condensed to a liquid boiling at $-102{\cdot}3$ and solidifying at $-169{\cdot}4°$. It is slightly soluble in water and in alcohol. When passed into bromine it is converted quickly into ethene bromide, $C_2H_4Br_2$ (148). It is absorbed readily by concentrated sulphuric acid at 170°, with formation of ethylsulphuric acid. SABATIER found a mixture of hydrogen and ethene to be changed completely into ethane by passage over finely-divided nickel at temperatures under 300° (28).

Pentenes or Amylenes, C_5H_{10}.

116. A mixture of isomeric pentenes and pentane is prepared technically by heating fusel-oil (43) with zinc chloride.

The isomeric pentenes can be separated by two methods, also applicable in other similar cases. One is based on the solution at a low temperature of some of the isomerides in a mixture of equal volumes of water and concentrated sulphuric acid, with formation of amylsulphuric acids, the other isomerides being insoluble. Simultaneously this process converts part of the amylenes into the condensation-products *diamylene* and *triamylene*. The other mode of separation depends on difference in the velocity of formation of addition-products between the isomeric pentenes and hydrogen iodide.

The Structure of Unsaturated Compounds.

117. Hitherto the existence of a double carbon bond in the alkenes has been assumed arbitrarily, but other modes of representing the constitution of unsaturated compounds are possible.

1. *Existence of bivalent or tervalent carbon atoms:*

$$CH_3-\overset{II}{C}-CH_3, \qquad \overset{III}{C}H_2-\overset{III}{C}H-CH_3.$$

2. *Existence of free bonds:*

a. On one carbon atom only:

$$CH_3-\underset{\wedge}{C}-CH_3.$$

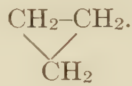
b. On different carbon atoms:

$$\underset{}{CH_3}—\underset{|}{CH}—\underset{|}{CH_2}.$$

3. *Existence of a double carbon bond:*

$$CH_3—CH{=}CH_2.$$

4. *Existence of a closed chain or ring:*



In 113, unsaturated compounds are stated to be convertible into saturated compounds by addition of atoms or groups. The constitution of these addition-products, coupled with the formation of unsaturated products by the elimination from the saturated compounds of hydrogen halide and other substances, facilitates decision between these four possibilities.

The same addition-product would be formed with a bivalent carbon atom as with two free bonds on the same carbon atom. Assuming propene to have either the constitution $CH_3\cdot\overset{II}{C}\cdot CH_3$ or $CH_3\cdot\underset{\wedge}{C}\cdot CH_3$, the addition of bromine produces the same substance, $CH_3\cdot CBr_2\cdot CH_3$. Similarly, the assumption of tervalent carbon atoms, or of free bonds on different carbon atoms, leads to the same result; $\overset{III}{C}H_2\cdot\overset{III}{C}H_2$ with two tervalent carbon atoms, and $\underset{|}{CH_2}\cdot\underset{|}{CH_2}$ with free bonds, yielding with bromine the same addition-product, $CH_2Br\cdot CH_2Br$. In view of these facts, at this stage it is unnecessary to consider cases 1 and 2 separately.

It is proved readily that addition does not take place only at a single carbon atom of unsaturated compounds, or ethene chloride, $C_2H_4Cl_2$, would have the constitution $CH_3\cdot CHCl_2$, and ethene itself, $CH_3\cdot CH$. Ethene chloride would be identical with the product obtained by the action of phosphorus pentachloride on acetaldehyde, $CH_3\cdot CHO$, for exchange of the oxygen atom of the aldehyde for two chlorine atoms yields a compound of the formula $CH_3\cdot CHCl_2$. Ethene chloride is different from the compound $C_2H_4Cl_2$ (*ethylidene chloride*)

got from acetaldehyde. Similarly, propene chloride, $C_3H_6Cl_2$, formed by the addition of chlorine to propene, is not identical with the reaction-product obtained from acetone and phosphorus pentachloride, $CH_3 \cdot CCl_2 \cdot CH_3$ (*chloroacetone*), nor with that from propionaldehyde, $CH_3 \cdot CH_2 \cdot CHCl_2$ (*propylidene chloride*). Ethene therefore cannot have either the formula $CH_3 \cdot CH$ or $CH_3 \cdot \overset{II}{C}H$, nor propene any of the formulæ $CH_3 \cdot C \cdot CH_3$, $CH_3 \cdot CH_2 \cdot CH$, $CH_3 \cdot \overset{II}{C} \cdot CH_3$, or $CH_3 \cdot CH_2 \cdot \overset{II}{C}H$.

118. A further insight into the structure of the unsaturated compounds is derived from other considerations. Propene is obtained by the elimination of hydrogen iodide from *n*-propyl iodide, $CH_3 \cdot CH_2 \cdot CH_2I$. The same compound is produced by similar abstraction from *iso*propyl iodide, $CH_3 \cdot CHI \cdot CH_3$. Accordingly propene cannot have either the formula $CH_2 \cdot CH_2 \cdot CH_2$ or $\begin{matrix} CH_2\text{–}CH_2 \\ \diagdown\!\diagup \\ CH_2 \end{matrix}$, the remaining possibilities being $CH_3 \cdot \overset{III}{C}H \cdot CH_2$, $CH_3 \cdot \overset{III}{C}H \cdot CH_2$, and $CH_3 \cdot CH : CH_2$.

iso*Butene*, C_4H_8, is formed similarly by the elimination of hydrogen iodide from either iso*butyl iodide*, $(CH_3)_2C\boxed{H}\underline{CH_2}\boxed{I}$, or *tertiary butyl iodide*, $(CH_3)_2C\boxed{I}\underline{\cdot CH_2}\boxed{H}$, indicating it to have one of the formulæ $(CH_3)_2C \cdot CH_2$, $(CH_3)_2\overset{III}{C} \cdot \overset{III}{C}H_2$, and $(CH_3)_2C : CH_2$. *Each example proves the removal of hydrogen halide from an alkyl halide to consist in the elimination of a halogen atom and a hydrogen atom attached to two carbon atoms in direct union*

Other examples serve as further illustrations of this principle. In accordance with it, removal of hydrogen iodide from a pentyl iodide, $\begin{matrix} CH_3 \\ C_2H_5 \end{matrix}\!>\!CH \cdot CH_2I$, should yield a *pentene*, C_5H_{10}, with the constitution, $\begin{matrix} CH_3 \\ C_2H_5 \end{matrix}\!>\!C \cdot CH_2$. Theory and fact agree, for the addition-product of the action of hydrogen iodide on this pentene is not the original pentyl iodide, but one with the formula $\begin{matrix} CH_3 \\ C_2H_5 \end{matrix}\!>\!CI \cdot CH_3$, as is established by replacement of iodine by hydroxyl, and comparison of the tertiary alcohol obtained with that of the same formula prepared by the synthetic method described in **102.**

The constitution of another pentyl iodide, $(CH_3)_2CH \cdot CH_2 \cdot CH_2I$, convertible into a pentene, C_5H_{10}, by elimination of hydrogen iodide, can be established similarly. With hydrogen iodide this pentene yields another pentyl iodide, $(CH_3)_2CH \cdot CHI \cdot CH_3$. The constitution of this compound is proved by its conversion into an alcohol oxidizable to a ketone, and therefore secondary.

Butlerow proved the impossibility of removing hydrogen halide from compounds with the halogen atom and the hydrogen atom not united with carbon atoms in juxtaposition. By addition of two bromine atoms he converted *iso*butene, $(CH_3)_2C{:}CH_2$, into $(CH_3)_2CBr \cdot CH_2Br$. Elimination of hydrogen bromide from this dibromide produced $(CH_3)_2C{:}CHBr$, its constitution being inferred from its oxidation to acetone:

$$(CH_3)_2C|{:}CHBr \longrightarrow (CH_3)_2CO.$$

It was not possible again to eliminate hydrogen bromide from *monobromobutene*, $(CH_3)_2C{:}CHBr$, no hydrogen being attached to the carbon atom in direct union with the CHBr-group.

119. The arguments advanced have reduced to three the constitutional formulæ possible for the unsaturated hydrocarbons.

1. Two free bonds on two carbon atoms directly attached:

$$\begin{array}{l} R \cdot CH \cdot CH \cdot R'. \\ \quad\ |\quad\ | \end{array}$$

2. Tervalent carbon atoms in direct union: $R \cdot \overset{\text{III}}{C}H \cdot \overset{\text{III}}{C}H \cdot R'$.
3. A double bond between two carbon atoms: $R \cdot CH{:}CH \cdot R'$.

For several reasons the preference is given to the formula with the double bond. First, it would be remarkable if only carbon atoms in juxtaposition could have free bonds or be tervalent. Second, experience has demonstrated the total lack of unsaturated compounds with an uneven number of free bonds or with tervalent carbon atoms. Next to the saturated hydrocarbons C_nH_{2n+2}, come in order of the number of hydrogen atoms, C_nH_{2n}, C_nH_{2n-2}, etc. Hydrocarbons, C_nH_{2n+1}, C_nH_{2n-1}, etc., with one or three free bonds, or with tervalent carbon atoms, are unknown, all attempts to isolate such products as methyl, CH_3, and ethyl, C_2H_5, having failed. The facts afford no support for the assumption of the existence either of free bonds or of tervalent carbon atoms. In addition the development of a double linking involves the elimination of hydrogen halide from adjoining carbon atoms in direct union, and excludes the possibility of the formation of such compounds as C_nH_{2n+1}. Only the assumption of the existence of the double bond explains the observed facts.

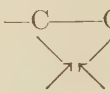
By analogy the lack of free bonds in the unsaturated hydrocarbons indicates their absence from other compounds containing atoms doubly linked, trebly linked, and so on. Such atoms are exemplified by nitrogen in the nitriles and oxygen in the ketones.

120. At first sight the assumption of the existence of multiple bonds presents certain difficulties connected with the power possessed by all such compounds of forming addition-products. As has been stated several times, carbon bonds are not severed easily (**36**), but the double carbon bond is converted very readily into a single bond through the formation of an addition-product. The invariable severance of a chain at its double carbon bond by oxidation presents an even more remarkable phenomenon. A satisfactory explanation of it is afforded by the frequent possibility of proving the absence of a direct rupture of the carbon chain at the double bond, an initial addition-product being formed by the taking up of two hydroxyl-groups:

Many such derivatives have been isolated. Oxidation continues always at the point of its initial inception (**45**), and further oxidation of such a compound must cause a severance of the carbon chain at the position previously occupied by the double bond. The rupture of the unsaturated chain by oxidation therefore involves the formation of an intermediate addition-product, and an explanation of the ease of the addition can be derived from a consideration of the nature of the bonds between the atoms. An affinity or bond can be regarded as an attraction exerted by one atom on another. For an atom with more than one affinity, the attraction is assumed to be exerted in more than one direction, and to be concentrated at certain points of its surface, as that of a magnet is localized at its two poles. Any other assumption, such as the equal distribution of the attracting force over the whole surface of an atom, would involve a difficulty with respect to the possession by each element of a determinate valency. If quadrivalent, the carbon atom must have on its surface four such points or "poles," situated at the angles of a regular tetrahedron (**48**). With a single bond between two such poles on different carbon atoms, their mutual attraction causes the atoms to approach one another as closely as possible.

VON BAEYER has suggested the mobility of these poles on the surface of carbon atoms, this characteristic inducing a degree of "strain" tending to make the poles revert to their original position. The con-

version of a single bond between two carbon atoms into a double bond must cause an appreciable alteration in the directions of the affinities of each carbon atom,



The resulting strain is a cause of the facile rupture of the double bonds. VON BAEYER'S *strain theory* affords an explanation of other important phenomena also.

Evidently the double bond must not be regarded as a mere duplication of the single bond, as the expression "double bond" might be supposed to indicate.

As has been demonstrated, the presence of a double bond exerts a great influence on chemical properties, but its effect on physical properties is no less marked. This phenomenon has been investigated most fully in connexion with refraction.

The molecular refractions (**26**) of a large number of unsaturated compounds containing a double bond and of the corresponding saturated derivatives have been determined by EYKMAN. His results indicate the *molecular dispersion* $\gamma-\alpha$, or the difference between the molecular refraction for the α-line of the hydrogen spectrum and that for the γ-line, to be appreciably greater for unsaturated compounds than for the corresponding saturated derivatives. This phenomenon is exemplified by the molecular refraction of C_6H_{14}. For the α-line it is 65·214, and for the γ-line 66·913, the dispersion being 1·699. For C_6H_{12} the value for the α-line is 64·814, and that for the γ-line is 67·027, the dispersion according to EYKMAN'S formula being 2·213.

The difference between the molecular refraction of a saturated compound and that of the corresponding unsaturated compound with two hydrogen atoms less in its molecule is denoted by $[H_2]$. Its value for the α-line of the hydrogen spectrum, employing EYKMAN'S formula, may lie between 1·0 and 0·2. Further investigation has proved this variation to depend on the number of carbon atoms in direct union with the group $>C{=}C<$. For $[H_2]_1$, corresponding with direct union of one carbon atom with the group $>C{=}C<$, the mean value has been found to be 0·96; for $[H_2]_2$, corresponding with two carbon atoms in direct union, it is 0·59; and for $[H_2]_3$ it is 0·24. These examples illustrate the aid furnished by refractometry in locating the position in the molecule occupied by a double bond.

There is an important difference between the molecular refraction of a hydrocarbon C_nH_{2n} and that of $(CH_2)_n$. The value corresponding with

CH_2 for the α-line is given in **33** as 10·260. The molecular refraction α for C_6H_{12} is 64·814, that for $(CH_2)_6$ being 61·56. The presence of the double linking causes an increase of the refraction, known as the *increment* of the double bond.

II. ALICYCLIC COMPOUNDS OR CYCLANES, C_nH_{2n}.

121. Isomeric with the olefines is a series of compounds, C_nH_{2n}, distinguished chiefly by the absence of, or at least a diminution in, the power of forming addition-products. Most of these compounds are very stable, *cyclo*pentane, C_5H_{10}, closely resembling *n*-pentane, C_5H_{12}. The methods for the formation of these compounds make evident the existence of a ring or closed carbon chain in the molecule (**275–280**).

III. HYDROCARBONS, C_nH_{2n-2}.

122. Two structures are possible for the hydrocarbons with four hydrogen atoms less than the corresponding paraffins. Hydrocarbons with two double bonds have the general formula C_nH_{2n-2}, exemplified by

$$CH_2{:}CH{\cdot}CH{:}CH_2.$$
Vinylethene

Other substances with a *triple bond* have the same general formula, such as

$$CH_3{\cdot}C{\equiv}CH.$$
Allylene

For reasons similar to those applicable to the double bond in the alkenes (**119**), the triple linking is assumed to be present in these compounds.

A. HYDROCARBONS WITH TRIPLE BONDS.

Nomenclature.

123. The first member, C_2H_2, is termed *acetylene*, and the second, C_3H_4, *allylene*. The higher members are regarded as substituted acetylenes, C_4H_6 being named *ethylacetylene*, C_6H_{10} *butylacetylene*, and so on. Their alternative names are formed by changing the termination "ane" of the saturated hydrocarbons into "yne," C_2H_2 being *ethyne*, and so on.

Methods of Formation.

1. By the dry distillation of complex compounds such as coal, acetylene being a constituent of coal-gas.

2. By the withdrawal of two molecules of hydrogen halide from

compounds of the formula $C_nH_{2n}X_2$, X representing a halogen atom, these compounds being formed by the addition of halogen to alkenes:

$$\underset{\text{Ethene bromide or 1 : 2-Dibromoethane}}{CH_2Br—CH_2Br} - 2HBr = \underset{\text{Acetylene or Ethyne}}{CH{\equiv}CH}.$$

The elimination of hydrogen halide is effected by heating with alcoholic potash.

A general method for the preparation of unsaturated compounds is furnished by this method of adding halogen, followed by the removal of hydrogen halide. From C_nH_{2n+2}, $C_nH_{2n+1}X$ can be obtained by the action of chlorine or bromine. Heating with alcoholic potash converts this product into C_nH_{2n}; from it $C_nH_{2n}Br_2$ is got by the action of bromine, and is converted into C_nH_{2n-2} by abstraction of two molecules of hydrogen bromide. This compound can form another addition-product with bromine, and so on.

3. By the elimination of two molecules of hydrogen halide from compounds of the formula $C_nH_{2n}X_2$, produced by the action of phosphorus pentahalide on aldehydes or ketones:

$$\underset{\text{Ethylidene chloride or 1 : 1-Dichloroethane}}{CH_3 \cdot CHCl_2} - 2HCl = \underset{\text{Acetylene or Ethyne}}{CH{\equiv}CH}.$$

$$\underset{\text{2 : 2-Dichloropropane}}{CH_3 \cdot CCl_2 \cdot CH_3} - 2HCl = \underset{\text{Allylene or Propyne}}{CH_3 \cdot C{\equiv}CH}.$$

124. Some of the hydrocarbons prepared by these methods exhibit a characteristic behaviour towards an ammoniacal solution of cuprous chloride or of a silver salt, a property facilitating their recognition. By replacement of hydrogen, they yield metallic derivatives as a voluminous precipitate insoluble in the ammoniacal solution or in water. These compounds are explosive, that derived from copper being yellow or red, and that from silver white. Acetylene, and its higher homologues derived from the dihalogen compounds of the aldehydes, yield metallic compounds of the type C_2Cu_2. The method of formation of these homologues proves them to contain the group ≡CH:

$$C_nH_{2n+1} \cdot CH_2 \cdot CHO \rightarrow C_nH_{2n+1} \cdot CH_2 \cdot CHCl_2 \rightarrow C_nH_{2n+1} \cdot C{\equiv}CH.$$

This fact indicates the presence of the group ≡CH *to be essential to the production of metallic derivatives*, the hydrogen of this group being that replaced by metals. Only the dichloro-derivatives of the methyl-ketones (**101**) can be transformed into hydrocarbons yielding metallic compounds, a fact supporting this view:

$$C_nH_{2n+1}\cdot CO\cdot CH_3 \rightarrow C_nH_{2n+1}\cdot CCl_2\cdot CH_3 \rightarrow \underset{\text{Yields metallic derivatives}}{C_nH_{2n+1}\cdot C\equiv CH};$$

$$C_2H_5\cdot CO\cdot C_2H_5 \rightarrow C_2H_5\cdot CCl_2\cdot CH_2\cdot CH_3 \rightarrow \underset{\text{Does not yield metallic derivatives}}{C_2H_5\cdot C\equiv C\cdot CH_3}.$$

The isomeric hydrocarbons containing two double bonds (**127**) also are incapable of forming metallic compounds.

The hydrocarbons are liberated readily from their metallic derivatives by dilute hydrochloric acid. This reaction affords a means of isolating from mixtures the members of the series C_nH_{2n-2} capable of yielding such derivatives, and of obtaining them in the pure state.

125. The hydrocarbons of this series can combine with four halogen atoms or with two molecules of a hydrogen halide. In presence of mercury salts they can take up water, forming aldehydes or ketones:

$$CH\equiv CH+H_2O=CH_3\cdot CHO;$$

$$CH_3\cdot C\equiv CH+H_2O=CH_3\cdot CO\cdot CH_3.$$

Mercury compounds are formed initially by addition, allylene, C_3H_4, passed into a solution of mercuric chloride first forming a precipitate of the composition $3HgCl_2,3HgO,2C_3H_4$, convertible into acetone by the action of hydrochloric acid.

The hydrocarbons of the acetylene series also yield condensation-products. Sometimes the condensation is between three molecules, acetylene, C_2H_2, giving benzene, C_6H_6; dimethylacetylene, C_4H_6, changing to hexamethylbenzene, $C_{12}H_{18}$; etc. This transformation is effected by the action of heat on acetylene, and of sulphuric acid on its homologues.

Acetylene or Ethyne, C_2H_2.

126. Acetylene is a colourless gas of disagreeable odour, is somewhat soluble in water, and condenses at 18° and 83 atmospheres to a liquid boiling at −82.4°. It can be synthesized from its elements by the aid of an electric-arc discharge between carbon poles in an atmosphere of hydrogen, but the maximum yield of acetylene at 2,500° is only 3·7 per cent. At the same temperature, about 1·2 per cent. of methane and a trace of ethane are formed simultaneously. The presence of acetylene can be detected by means of an ammoniacal solution of cuprous chloride, a red precipitate of copper acetylene being produced even from traces of acetylene mixed with other gases. Acetylene is a product of the incomplete combustion of many organic

substances. It is prepared on the large scale by the action of water on calcium carbide, or calcium acetylene, CaC_2:

$$CaC_2 + 2H_2O = Ca(OH)_2 + C_2H_2.$$

The reaction is somewhat violent, and is attended by the evolution of considerable heat. Calcium carbide is prepared by heating carbon with quicklime, CaO, in an electric furnace. Under the influence of the high temperature, the calcium liberated by the action of the carbon on the quicklime combines with the excess of carbon to form calcium carbide. The pure substance is white, but the ordinary product has a dark reddish-brown colour due to the presence of a small proportion of iron.

Various applications of acetylene have been facilitated by the cheap and simple method of preparation from calcium carbide. A solution in acetone is employed usually in the arts and manufactures, the gas being compressed at twelve atmospheres into steel cylinders containing this solvent. At this pressure, one volume of acetone dissolves about three hundred volumes of acetylene. Ignition of the gas evolved from this solution through a fine orifice gives a bright luminous flame free from smoke, employed as an illuminant in buildings, railway-carriages, motor-car and bicycle lamps, gas-buoys, and so on. When acetylene is burnt in oxygen a temperature approximating to 3,500° is generated, and this property finds application in *autogenous welding*, an oxy-acetylene blowpipe developing sufficient heat to melt iron readily. Steel plates for safes, rails for railway or tramway use, and other iron or steel material can be welded readily by its aid. Thick iron plates can be cut through by employing an oxy-acetylene blowpipe to raise their temperature at one point to white heat, and then cutting off the supply of acetylene and moving the oxygen tube along the plate. The oxygen converts the metal into oxide, and the temperature of the oxide in proximity to the current of gas is raised by the heat of combustion to fusion. Consequently, this oxide drops in liquid form, a sharp and clean cut being effected.

Another important application of acetylene is its conversion into acetaldehyde. As stated in 125, under the influence of mercury salts this hydrocarbon can take up the elements of water. The process is developed sufficiently to be of technical application, the acetaldehyde admitting of reduction to ethyl alcohol, and of oxidation to acetic acid.

B. HYDROCARBONS WITH TWO DOUBLE BONDS.

127. *Isoprene*, C_5H_8, is a hydrocarbon of this series, and is of great importance on account of its close relation to caoutchouc (370). In recent years many attempts have been made to prepare isoprene technically, some with success. A very good laboratory-method for its

preparation is mentioned in 367. A poor yield of the hydrocarbon is obtained by the dry distillation of caoutchouc. It is a liquid boiling at 37°, and has the density $D_4^{21} = 0{\cdot}6793$. Isoprene is proved to have the constitution $\begin{matrix}CH_2\\CH_3\end{matrix}\!\!>\!C\cdot CH{=}CH_2$ by its conversion through addition of two molecules of hydrogen bromide into a dibromide, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CBr{-}CH_2{-}CH_2Br$, identical with that obtained from dimethylallene, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C{=}C{=}CH_2$.

In the preparation of *dimethylallene*, the two carbinol-derivatives, dimethylethylcarbinol $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C(OH)\cdot CH_2\cdot CH_3$, and methyl*iso*propylcarbinol, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH\cdot CHOH\cdot CH_3$, are got by the method described in 102, and converted into the corresponding iodides. On elimination of hydrogen iodide, each iodide yields trimethylethene, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C{=}CH\cdot CH_3$, its formation from both iodides admitting of no other position for the double bond. Trimethylethene takes up two atoms of bromine, forming $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CBr\cdot CHBr\cdot CH_3$. Alcoholic potash reacts with this substance, eliminating two molecules of hydrogen bromide, and forming dimethylallene, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C{=}C{=}CH_2$.

This mode of formation does not preclude wholly another arrangement of the double bonds, but other evidence proves dimethylallene to have the structural formula indicated.

1. On oxidation it yields acetone, indicating the presence of the group $(CH_3)_2C{=}$.

2. Sulphuric acid of fifty per cent. strength converts it into methyl*iso*propylketone:

$$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C{=}C{=}CH_2 + 2H_2O = \underset{\text{Intermediate product}}{\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH\cdot C(OH)_2\cdot CH_3} \rightarrow$$

$$\rightarrow \begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH\cdot COCH_3.$$

Compounds like this intermediate product are mentioned in 149, 201, 204, 230 and 234.

In forming an addition-product with two univalent atoms, organic compounds containing the group C=C—C=C, termed by THIELE a "Conjugated system," often behave peculiarly, the addition taking

place at carbon atoms 1 and 4, with formation of a double bond between carbon atoms 2 and 3:

$$CH_2{=}CH\cdot CH{=}CH_2 + Br_2 = CH_2Br\cdot CH{=}CH\cdot CH_2Br.$$

The subject of conjugated double bonds is discussed further in **287.**

Compounds with a conjugated system of double bonds also exhibit characteristic physical properties. A comparison of their molecular refractions with those of the corresponding saturated compounds, or with those of substances containing only a single double linking, shows them to be much higher for conjugated compounds than would be anticipated from the presence of two double bonds. This phenomenon is termed the *exaltation* of the conjugated system, and its existence affords a means of deciding whether two double bonds are conjugated or not.

SUBSTITUTION-PRODUCTS OF THE UNSATURATED HYDROCARBONS.

I. UNSATURATED HALOGEN COMPOUNDS.

128. The saturated hydrocarbons not possessing any salient characteristics, the properties of their compounds depend on the nature of the substituents. Hitherto, only compounds with properties due to the presence in the molecule of a single group, such as hydroxyl, carboxyl, or a multiple carbon bond, have been described. At this stage substances containing more than one characteristic group in the molecule must be considered.

The presence of such groups simultaneously in the same molecule modifies their properties. The extent of this influence varies considerably, as is made evident by consideration of the different classes of *unsaturated halogen compounds.*

Halogen derivatives of the type $C_nH_{2n-1}X$ are obtained by the addition of halogen to the hydrocarbons C_nH_{2n}, and subsequent elimination of one molecule of hydrogen halide:

$$CH_2{=}CH_2 + Br_2 = CH_2Br{-}CH_2Br.$$

$$CH_2Br{-}CH_2Br - HBr = CH_2{=}CHBr.$$

Ethene bromide — Vinyl bromide or Bromoethene

They are formed also by removal of one molecule of hydrogen halide from compounds containing two halogen atoms in union with the same carbon atom:

$$CH_3 \cdot CH_2 \cdot CHCl_2 - HCl = CH_3 \cdot CH{=}CHCl.$$

Propylidene chloride or 1 : 1-Dichloropropane — 1-Chloropropene-1

$$CH_3 \cdot CCl_2 \cdot CH_3 - HCl = CH_3 \cdot CCl{=}CH_2.$$

2 : 2-Dichloropropane — 2-Chloropropene-1

The methods employed in the preparation of these compounds indicate their halogen atom to be in union with a carbon atom having a double bond. Their properties differ widely from those of compounds

like the alkyl halides with the halogen atom attached to a singly-linked carbon atom, this rule being general for such compounds. The halogen atoms of the alkyl halides are adapted especially to double decompositions, being replaceable by hydroxyl, an alkoxyl-group, an acid-residue, the amino-group, and so on.

This aptitude for double decomposition is almost lacking in compounds with halogen in union with a doubly-linked carbon atom. Alkalis do not convert them into alcohols, nor alkoxides into ethers, any reaction invariably involving elimination of hydrogen halide with formation of hydrocarbons of the series C_nH_{2n-2}.

129. An isomeride of the 1-*chloropropene*-1 and 2-*chloropropene*-1 already mentioned is termed *allyl chloride.* Its halogen atom takes part in double decompositions as readily as the halogen atom of an alkyl chloride. Allyl chloride is obtained by the action of phosphorus pentachloride on allyl alcohol, $CH_2{:}CH\cdot CH_2OH$ (**132**). This alcohol yields *n*-propyl alcohol by addition of hydrogen, and therefore its hydroxyl-group must be at the end of the carbon chain. The halogen atom in allyl chloride also must be at the end of the chain, as it replaces the hydroxyl-group. Given the constitutions of 1-chloropropene-1 and 2-chloropropene-1, deducible from those of propionaldehyde and acetone, the allyl halides can have only the constitutional formula

$$CH_2{=}CH\cdot CH_2X.$$

The halogen atom is attached to a singly-linked carbon atom, and retains its normal character despite the presence of a double bond in the molecule.

The influence exerted on the character of a halogen atom by its position in the molecule of an unsaturated compound affords a means of determining whether it is attached to a singly-linked or doubly-linked carbon atom, the indication being its possession or lack of the power to take part in double decompositions.

Examples of individual members of the series are the gaseous *vinyl chloride,* $CH_2{:}CHCl$, and the liquid *vinyl bromide,* $CH_2{:}CHBr$, characterized by its ethereal odour. Each of these compounds polymerizes readily.

130. *Allyl chloride, allyl bromide,* and *allyl iodide,* boil respectively at 46°, 70°, and 103°. They are employed often in syntheses to introduce an unsaturated group into a compound. They have a characteristic odour resembling that of mustard.

The *propargyl compounds,* $CH{\equiv}C\cdot CH_2X$, are typical of the series $C_nH_{2n-3}X$. Their constitution is inferred from their power of yielding metallic derivatives, indicating the presence of the group $\equiv CH$; and

from the capacity of their halogen atoms for double decomposition, proving their union with a singly-linked carbon atom. They are obtained from propargyl alcohol (133) by the action of phosphorus pentahalides, and are liquids of pungent odour.

Bromoethyne, CHBr : C, is assumed by Nef to contain a bivalent carbon atom. It can be obtained from 1:2-dibromoethene, CHBr : CHBr, by means of alcoholic potash. It is a gas, boils at −2°, and takes fire spontaneously in the air. Owing to slow oxidation its solution in alcohol is phosphorescent, and the gas has an odour very similar to that of phosphorus.

II. UNSATURATED ALCOHOLS.

131. The hydroxyl-group of the *unsaturated alcohols* may be attached to a singly-linked or a doubly-linked carbon atom:

$CH_2{:}CH{\cdot}CH_2OH$, 2-Propenol-1 or Allyl alcohol $CH_2{:}CH{\cdot}OH$. Ethenol or Vinyl alcohol

Few compounds of the type of *vinyl alcohol* are known, reactions such as might be expected to yield them generally producing their isomerides. Abstraction of water from glycol, $CH_2OH{\cdot}CH_2OH$, does not give vinyl alcohol, $CH_2{=}CHOH$, but the isomeric acetaldehyde, $CH_3{-}C\langle^{H}_{O}$.

2-Bromopropene-1, $CH_3{\cdot}CBr{:}CH_2$, is not changed into 2-hydroxypropene-1, $CH_3{\cdot}C(OH){:}CH_2$, by heating with water, but into the isomeric acetone, $CH_3{\cdot}CO{\cdot}CH_3$. The usual rule is for an anticipated grouping of the atoms in the form —CH:C(OH)— to undergo a transformation into $—CH_2{\cdot}CO—$. Most substances with hydroxyl attached to a doubly-linked carbon atom are unstable and tend to change into isomerides, but compounds containing a stable group —CH:C(OH)— (235 and 236) do exist.

Neurine is a vinyl-derivative of great physiological importance. It is formed in the putrefactive decay of flesh and in other fermentation-processes. Its constitution is $(CH_3)_3N{<}^{CH:CH_2}_{OH}$, as is indicated by its synthesis. Trimethylamine reacts with ethylene bromide to yield a substituted ammonium bromide of the formula $(CH_3)_3N{<}^{CH_2{\cdot}CH_2Br}_{Br}$. Moist silver oxide eliminates one molecule of hydrogen bromide from the group $—CH_2{\cdot}CH_2Br$, the bromine atom attached to nitrogen being replaced simultaneously by hydroxyl. A substance of the constitution indicated is obtained, and in all respects is similar to neurine.

2-Propenol-1 or Allyl Alcohol, $CH_2{:}CH\cdot CH_2OH$.

132. Many unsaturated alcohols containing hydroxyl attached to a singly-linked carbon atom are known. The most important is *allyl alcohol*, prepared by the method described in 163. Its constitution is inferred from that of the chlorine derivative formed by the action of phosphorus pentachloride (129), and also from the oxidation of allyl alcohol to an aldehyde, *acraldehyde*, and then to *acrylic acid:*

$$\underset{\text{Allyl alcohol}}{CH_2{:}CH\cdot CH_2OH} \rightarrow \underset{\text{Acraldehyde}}{CH_2{:}CH\cdot C\begin{matrix}\diagup H\\ \diagdown\!\!\diagdown O\end{matrix}} \rightarrow \underset{\text{Acrylic acid}}{CH_2{:}CH\cdot COOH.}$$

These reactions prove allyl alcohol to contain the group $—CH_2OH$ characteristic of primary alcohols.

Allyl alcohol is a liquid of irritating odour, solidifies at $-50°$, boils at $96\cdot5°$, and is miscible with water in all proportions. At $0°$ its density is $0\cdot872$. It forms addition-products with the halogens, and with hydrogen yields *n*-propyl alcohol.

Many other compounds with the allyl-group, $CH_2{:}CH\cdot CH_2—$, are known, among them *allyl sulphide* $(CH_2{:}CH\cdot CH_2)_2S$, the principal constituent of oil of garlic. It is obtained synthetically by the action of potassium sulphide, K_2S, on allyl iodide.

Obviously the influence of a double bond situated in the immediate neighbourhood of the halogen or hydroxyl of unsaturated halogen compounds and alcohols is very pronounced, but that of one placed elsewhere is much less marked. *Two groups situated in immediate proximity in the same molecule exert a strong influence on the properties of each other.*

2-Propynol-1 or Propargyl Alcohol, $CH{\equiv}C\cdot CH_2OH$.

133. *Propargyl alcohol* contains a triple bond, and is prepared from tribromohydrin or 1:2:3-tribromopropane, $CH_2Br\cdot CHBr\cdot CH_2Br$. Potassium hydroxide converts this substance into $CH_2{:}CBr\cdot CH_2Br$, transformed by potassium acetate and saponification into $CH_2{:}CBr\cdot CH_2OH$, only the terminal bromine atom being capable of taking part in double decomposition (128). Contact with potassium hydroxide of the alcohol produced eliminates another molecule of hydrogen bromide with formation of propargyl alcohol, its constitution being indicated by this method of formation and also by its properties. The presence of the group $\equiv CH$ is proved

by the formation of metallic derivatives. On oxidation it yields *propiolic acid*, $CH{\equiv}C{\cdot}COOH$, with the same number of carbon atoms, revealing it to be a primary alcohol.

Propargyl alcohol is a liquid of agreeable odour, is soluble in water, and boils at 114°–115°. At 21° its density is 0·963. Its metallic derivatives are explosive.

UNSATURATED MONOBASIC ACIDS.

I. ACIDS OF THE OLEIC SERIES, $C_nH_{2n-2}O_2$.

134. The acids of the *oleic series* can be obtained from the saturated acids $C_nH_{2n}O_2$ by the methods generally applicable to the conversion of saturated substances into unsaturated compounds.

1. Substitution of one hydrogen atom in the alkyl-group of a saturated acid by a halogen atom, and subsequent elimination of hydrogen halide by heating with alcoholic potash.

2. Removal of the elements of water from the monohydroxy-acids:

$$\underset{\text{2-Hydroxybutyric acid}}{CH_3 \cdot CHOH \cdot CH_2 \cdot COOH} - H_2O = \underset{\text{Crotonic acid}}{CH_3 \cdot CH{:}CH \cdot COOH}.$$

The acids of this series can be prepared also from unsaturated compounds by

3. Oxidation of the unsaturated alcohols and aldehydes.

4. The action of potassium cyanide on unsaturated halogen compounds such as allyl iodide, and hydrolysis of the carbonitrile formed.

Nomenclature.

Most of the acids of the oleic series are named after their primary parent substances, but a few of the middle members have names indicating the number of carbon atoms in the molecule. The first member, $CH_2{:}CH \cdot COOH$, is termed *acrylic acid*: others are *crotonic acid*, $C_4H_6O_2$; *angelic acid and tiglic acid*, $C_5H_8O_2$; *undecylenic acid*, $C_{11}H_{20}O_2$; *oleic acid*, $C_{18}H_{34}O_2$; *erucic acid*, $C_{22}H_{42}O_2$; etc.

Their systematic names are formed by adding the words "Carboxylic acid" to the names of the corresponding hydrocarbons, $C_4H_6O_2$ being *propenecarboxylic acid*, and so on.

Properties.

135. In common with all compounds containing a double bond, the acids of this series possess the power of forming addition-products. They are "stronger" acids than the corresponding fatty acids with the same number of carbon atoms in the molecule, the value of the constant 10^4k (87) for propionic acid, $C_3H_6O_2$, being 0·134; for acrylic

acid, $C_3H_4O_2$, 0·56; for butyric acid, $C_4H_8O_2$, 0·149; and for crotonic acid, $C_4H_6O_2$, 0·204. The double bond renders the acids of the oleic series much more susceptible to oxidation than the members of the fatty series (**120**). Those of the first type are converted by energetic oxidizers into two saturated acids, but a reaction moderated by employing a dilute solution of potassium permanganate yields as an intermediate product a dihydroxy-acid containing the group —CHOH·CHOH—, and on further oxidation the chain is severed at the bond between these two carbon atoms (**120**). This behaviour affords a means of determining the position of the double bond in the molecule. A rupture of the molecule with formation of saturated fatty acids is effected also by fusion of an unsaturated acid with potassium hydroxide in presence of air:

$$\begin{array}{r|l} C_nH_{2n+1}\cdot CH: & CH\cdot COOH \\ KO & H \\ KO & H \\ O & \end{array} = C_nH_{2n+1}\cdot C\begin{array}{l} O\overline{H} \\ \overline{OK} \\ \overline{OK} \end{array} + CH_3\cdot COOH.$$

Formerly this reaction was employed to determine the location of the double bond, the division of the molecule being assumed to occur at the original position of this bond. Modern research has proved the position of the double bond to be displaced nearer that of the carboxyl-group under the influence of fused potassium hydroxide, or even by boiling with a solution of sodium hydroxide. Fusion with potassium hydroxide therefore cannot be employed to determine the position of double bonds. The action of ozone on these acids is described in **198**.

Ethanecarboxylic or Acrylic Acid, $CH_2{:}CH\cdot COOH$.

136. *Acrylic acid* is obtained by the elimination of one molecule of hydrogen iodide from 2-iodopropionic acid, $CH_2I\cdot CH_2\cdot COOH$. It is a liquid of pungent odour, solidifies at 12·3°, boils at 140°, and at 20° has the density 1·0511. It is reduced by nascent hydrogen to propionic acid.

Acids of the formula $C_4H_6O_2$.

The acids of the formula $C_4H_6O_2$ theoretically possible are

1. $CH_2{:}CH\cdot CH_2\cdot COOH$; 2. $CH_3\cdot CH{:}CH\cdot COOH$;

3. $CH_2{:}C\begin{cases} CH_3 \\ COOH \end{cases}$; 4. $\begin{array}{l} CH_2 \\ | \\ CH_2 \end{array}\!\!>CH\cdot COOH$;

but five acids of that formula are known.

An acid of the constitution indicated in formula 1, *propene-2-carboxylic*-1 or *vinylacetic acid*, can be obtained by the action of carbon dioxide on allyl magnesium bromide, and decomposition of the primary product by acidulated water:

$$CH_2{:}CH\cdot CH_2MgBr + CO_2 = CH_2{:}CH\cdot CH_2\cdot CO_2MgBr;$$

$$CH_2{:}CH\cdot CH_2\cdot CO_2MgBr + H_2O = CH_2{:}CH\cdot CH_2\cdot COOH + MgBr\cdot OH.$$

Its production by the action of potassium cyanide on allyl iodide and hydrolysis of the carbonitrile formed might be expected:

$$\underset{\text{Allyl iodide}}{CH_2{:}CH\cdot CH_2I} \rightarrow CH_2{:}CH\cdot CH_2CN \rightarrow CH_2{:}CH\cdot CH_2\cdot COOH.$$

Actually an acid of formula 2 is obtained, *solid crotonic acid*, melting at 71° and boiling at 180°. Careful oxidation with permanganate converts it into oxalic acid, HOOC—COOH, a proof of its constitution, and an indication of a change during the reaction in the position of the double bond.

Eykman proved allyl cyanide to have the formula $CH_2{:}CH\cdot CH_2\cdot CN$. The molecular refraction for the α-line based on his formula is

For propyl cyanide, $C_3H_7\cdot CN$	44·55
For allyl cyanide, $C_3H_5\cdot CN$	43·51
Difference	1·04

This difference corresponds with $[H_2]_1$, indicating the group $>C{=}C<$ to be in union with only a single carbon atom, and therefore situated at the end of the chain (**120**).

iso*Crotonic acid*, melting at 15·5° and boiling at 172°, also has constitution 2, it being reducible like solid crotonic acid to *n*-butyric acid, proving it also to contain a normal carbon chain, and being convertible by careful oxidation into oxalic acid. Ordinary constitutional formulæ are incapable, therefore, of accounting for the isomerism of these acids. An explanation of it is given in **169**.

An acid with formula 3 obtained by the elimination of one molecule of hydrogen bromide from bromo*iso*butyric acid is named *methacrylic acid*:

$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CBr\cdot COOH \rightarrow \begin{matrix} CH_2 \\ CH_3 \end{matrix}\!\!>\!C\cdot COOH.$$

The acid of formula 4 is mentioned in **275**.

Heptadecene-8-carboxylic-1 or Oleic Acid, $C_{18}H_{34}O_2$.

137. *Oleic acid* is obtained by the saponification of oils and soft fats (85). To separate it from the saturated stearic acid and palmitic acid simultaneously liberated, the lead salt is prepared. Lead oleate is soluble in ether, but lead palmitate and lead stearate are insoluble. The oleic acid is liberated from the lead oleate by the action of an acid.

At the ordinary temperature oleic acid is a liquid without odour and of an oily nature. It melts at 14°. In the air it oxidizes readily, and it cannot be distilled at the ordinary pressure without decomposition.

Oleic acid contains a normal carbon chain, since on reduction it yields stearic acid.

KRAFFT has proved the normal structure of stearic acid by converting it step by step into acids with a smaller number of carbon atoms. Dry distillation in a vacuum of a mixture of barium stearate and barium acetate forms a ketone, $C_{17}H_{35}\cdot CO\cdot CH_3$:

$$C_{17}H_{35}\cdot\boxed{COOba^* + baO\cdot}OC\cdot CH_3 \rightarrow C_{17}H_{35}\cdot CO\cdot CH_3.$$

Barium stearate — Barium acetate — Margarylmethylketone

On oxidation, this ketone yields acetic acid and an acid of the formula $C_{17}H_{34}O_2$. This reaction proves the ketone to contain a CH_2-group next to the carbonyl-group, and to have the formula $C_{16}H_{33}\cdot CH_2\cdot CO\cdot CH_3$, for only from such a compound could oxidation produce an acid with seventeen carbon atoms. This acid, $C_{17}H_{34}O_2$ (*margaric acid*), is transformed similarly into a ketone, $C_{16}H_{33}\cdot CO\cdot CH_3$, convertible by oxidation into an acid $C_{16}H_{32}O_2$. These facts prove the formula of margaric acid to be $C_{15}H_{31}\cdot CH_2\cdot COOH$, and that of stearic acid to be $C_{15}H_{31}\cdot CH_2\cdot CH_2\cdot COOH$. The acid $C_{16}H_{32}O_2$, *palmitic acid*, is in its turn converted into a ketone, and the process continued until *capric acid* $C_{10}H_{20}O_2$, is obtained. This acid has been proved by synthesis (**233**, 1) to contain a normal carbon chain.

The presence of a double bond in oleic acid is indicated by its forming an addition-product with bromine, and by its power of reducing an alkaline permanganate solution (**113**). The double bond is situated at the centre of the chain, the constitution of oleic acid being

$$CH_3\cdot(CH_2)_7\cdot CH{:}CH\cdot(CH_2)_7\cdot COOH.$$

This constitution is inferred from the conversion of the acid by careful oxidation into *octadecanecarboxylic*-1 or *pelargonic acid*, $C_8H_{17}\cdot COOH$, and *heptanedicarboxylic*-1:7 or *azelaic acid*, $HOOC\cdot(CH_2)_7\cdot COOH$.

* $\underline{ba} = \frac{1}{2}\underline{Ba}$.

138. Oleic acid reacts in a remarkable manner with even a mere trace of nitrous acid. The best method is to pass into oleic acid the red gaseous mixture of nitrogen peroxide and nitric oxide obtained by heating arsenious oxide with nitric acid, or to add nitric acid of density 1·25. The oleic acid soon solidifies, being converted into the isomeric *elaidic acid*. The reaction is termed the "Elaidic transformation." Other acids of this series are transformed similarly, *erucic acid*, $C_{22}H_{42}O_2$, being converted by a trace of nitrous acid into *brassidic acid*.

Elaidic acid has the same structural formula as oleic acid, the double bond occupying a similar position in the molecule of each, since each acid readily forms a bromine addition-product convertible by elimination of two molecules of hydrogen bromide into *stearolic acid*, $C_{18}H_{32}O_2$:

$$\underset{\text{Oleic and elaidic acids}}{C_{18}H_{34}O_2} \rightarrow \underset{\text{Bromine addition-product}}{C_{18}H_{34}Br_2O_2} \rightarrow \underset{\text{Stearolic acid}}{C_{18}H_{32}O_2}.$$

Oleic acid and elaidic acid yield the same hydroxystearic acid by the addition of one molecule of water, a reaction effected by the action of concentrated sulphuric acid. Like that of erucic acid and brassidic acid, their isomerism is therefore analogous to the isomerism of the two crotonic acids (**136**).

II. ACIDS OF THE PROPIOLIC SERIES, $C_nH_{2n-4}O_2$.

139. The acids of the *propiolic series* have one triple bond or two double bonds in the molecule. Substances of the first type are formed by the action of carbon dioxide on the sodium compounds of the acetylene hydrocarbons:

$$CH{\equiv}CNa + CO_2 = \underset{\text{Sodium propiolate or ethynecarboxylate}}{CH{\equiv}C\cdot COONa}.$$

The 1-carbon atom of these acids has a triple bond, and such acids are decomposed very readily into an acetylene hydrocarbon and carbon dioxide, one method being to heat their silver salts.

A general method for the preparation of acids with triple bonds involves the addition of two bromine atoms to acids containing a double bond, and subsequent elimination of two molecules of hydrogen bromide:

$$\underset{\text{Crotonic acid}}{CH_3\cdot CH{:}CH\cdot COOH} \rightarrow \underset{\text{Dibromobutyric acid}}{CH_3\cdot CHBr\cdot CHBr\cdot COOH} \rightarrow$$

$$\rightarrow \underset{\substack{\text{Propyne-1-carboxylic-1 or}\\ \text{Tetrolic acid}}}{CH_3\cdot C{\equiv}C\cdot COOH}.$$

140. In presence of concentrated sulphuric acid, substances with a triple bond take up water with formation of ketones (**125**):

$$—C{\equiv}C— \rightarrow —CH_2{\cdot}CO—.$$

In this manner stearolic acid is converted into a ketostearic acid of the formula

$$C_8H_{17}{\cdot}CO{\cdot}CH_2{\cdot}(CH_2)_7{\cdot}COOH,$$

and hydroxylamine transforms this compound into the corresponding oxime:

$$\begin{array}{l} C_8H_{17}{\cdot}\underset{\displaystyle\overset{\|}{NOH}}{C}{\cdot}CH_2{\cdot}(CH_2)_7{\cdot}COOH \end{array} .$$

Under the influence of concentrated sulphuric acid, this oxime undergoes the Beckmann transformation (**103**), among the products being the substituted acid amide

$$\begin{array}{l} C_8H_{17}{\cdot}CO \\ \qquad\quad | \\ \qquad\quad NH{\cdot}(CH_2)_8{\cdot}COOH \end{array},$$

proved to have this formula by its decomposition by fuming hydrochloric acid into pelargonic acid, $C_8H_{17}{\cdot}COOH$, and the 8-aminononylic acid, $NH_2{\cdot}(CH_2)_8{\cdot}COOH$. This reaction confirms the accuracy of the constitution assigned to oleic acid and elaidic acid, each being convertible into stearolic acid in the manner described.

Geranic acid, $C_{10}H_{16}O_2$, a compound with two double bonds, is considered in **143**.

UNSATURATED ALDEHYDES AND KETONES.

141. The simplest unsaturated aldehyde is *propenal*, or *acraldehyde*, or *acrolein*, $CH_2:CH\cdot CHO$. It is obtained by removal of water from glycerol (152), effected by heating at 195° one part of this substance with four parts of a mixture containing five parts of potassium hydrogen sulphate and one part of potassium sulphate. It is a colourless liquid, solidifies at −87°, boils at 52·4°, and at 15° has the density 0·8447. It has an extremely powerful and penetrating odour, the origin of its name (*acer*, sharp, and *oleum*, oil). The disagreeable pungent smell produced by extinguishing a tallow candle or an oil-lamp is due to the formation of acraldehyde. On reduction, it yields allyl alcohol, and is regenerated by careful oxidation of that alcohol. It is converted by further oxidation into acrylic acid.

It has the properties peculiar to aldehydes, including susceptibility to reduction and oxidation, resinification in presence of alkalis, and the power of forming polymerides. The last characteristic is so pronounced as usually to be displayed in complete polymerization in the course of a few days or even hours, probably under the catalytic influence of traces of impurities.

This polymeride is named *disacryl*. It is a colourless resin, and cannot be reconverted into propenal. The addition to propenal of traces of a polyhydric phenol such as quinol or pyrogallol was found by Moureu to inhibit both resinification and oxidation, rendering the substance stable. Sunlight has the opposite effect of accelerating the polymerization.

The presence of the double bond in acraldehyde modifies to some extent the aldehydic character, as is exhibited in its behaviour towards ammonia. With that substance it does not combine like acetaldehyde (104), but in accordance with the equation

$$2C_3H_4O+NH_3=C_6H_9ON+H_2O.$$

Acraldehydeammonia is an amorphous basic substance, is soluble in water, and in appearance and behaviour towards water closely resembles glue.

Acraldehyde does not unite with a single molecule of a primary sulphite, but with two molecules. The aldehyde cannot be regenerated from the product by the action of acids, only one molecule of the primary sulphite being eliminated. This reaction indicates the other molecule of primary sulphite to have been added at the double bond.

142. *Crotonaldehyde*, $CH_3 \cdot CH : CH \cdot CHO$, is a product of the elimination of water from aldol, $CH_3 \cdot CH(OH) \cdot CH(H) \cdot C{<}^{H}_{O}$ (**106**), effected by heating it at 140°. It is a liquid boiling between 104° and 105°, and is converted by oxidation with silver oxide into solid crotonic acid (**136**), proving it to have the constitution indicated.

Propiolaldehyde, $CH{\equiv}C \cdot C{<}^{H}_{O}$, can be obtained from acraldehydeacetal by the addition of two bromine atoms, and subsequent removal by means of potassium hydroxide of two molecules of hydrogen bromide from the addition-product formed:

$$\underset{\text{Acraldehydeacetal}}{CH_2 : CH \cdot C{<}^{H}_{(OC_2H_5)_2}} \rightarrow \underset{\text{Dibromo-compound}}{CH_2Br \cdot CHBr \cdot C{<}^{H}_{(OC_2H_5)_2}} \rightarrow$$

$$\rightarrow \underset{\text{Propiolaldehydeacetal}}{CH{\equiv}C \cdot C{<}^{H}_{(OC_2H_5)_2}}.$$

Propiolaldehydeacetal is converted by warming with dilute sulphuric acid into the corresponding aldehyde, a substance with an irritating action on the mucous membrane similar to that of acraldehyde.

The behaviour of propiolaldehyde towards alkalis is remarkable. It decomposes into acetylene and formic acid:

$$CH{\equiv}C \cdot CHO + NaOH = CH{\equiv}CH + C{<}^{H}_{ONa}{}_{O}.$$

143. An important unsaturated aldehyde is *geranial* or *citral*, $C_{10}H_{16}O$, characterized by its agreeable odour. It is a constituent of various essential oils; among them oil of orange-rind, the cheap oil of lemon-grass, and oil of citron. At the ordinary temperature it is liquid, and boils between 110° and 112° at a pressure of 12 mm. Its aldehydic nature is indicated by its reduction to the alcohol *geraniol*, and by its oxidation to *geranic acid* with the same number of carbon atoms.

Geranial is 3:7-dimethyl-$\Delta^{2:6}$-octadiene-1-al,

$$(CH_3)_2{>}C{=}CH \cdot CH_2 \cdot CH_2 \cdot C(CH_3){=}CH \cdot C{<}^{H}_{O},$$

for its oxidation yields acetone, lævulic acid (**234**), and carbon dioxide, the molecule rupturing at the double bonds:

$$\underset{\text{Geranial}}{(CH_3)_2{>}C{=}CH \cdot CH_2 \cdot CH_2 \cdot C(CH_3){=}CH \cdot C{<}^{H}_{O}} \rightarrow$$

$$\rightarrow \underset{\text{Acetone}}{(CH_3)_2{>}CO} + \underset{\text{Lævulic acid}}{HOOC \cdot CH_2 \cdot CH_2 \cdot CO \cdot CH_3} + \underset{\text{Carbon dioxide}}{CO_2} + CO_2.$$

When boiled with a solution of potassium carbonate, geranial takes up one molecule of water, forming *methylheptenone* and acetaldehyde:

$$\underset{\text{Geranial}}{\overset{CH_3}{\underset{CH_3}{>}}C{=}CH\cdot CH_2\cdot CH_2\cdot C(CH_3){=}CH\cdot C\overset{H}{\underset{O}{}}} \rightarrow$$

$$\rightarrow \underset{\text{Methylheptenone}}{\overset{CH_3}{\underset{CH_3}{>}}C{=}CH\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3} + \underset{\text{Acetaldehyde}}{CH_3\cdot C\overset{H}{\underset{O}{}}}.$$

Oxidation of methylheptenone also yields acetone and lævulic acid. This reaction indicates its constitution, additional evidence being furnished by its synthesis.

Baryta-water converts a mixture of geranial and acetone into the condensation-product pseudo*ionone*:

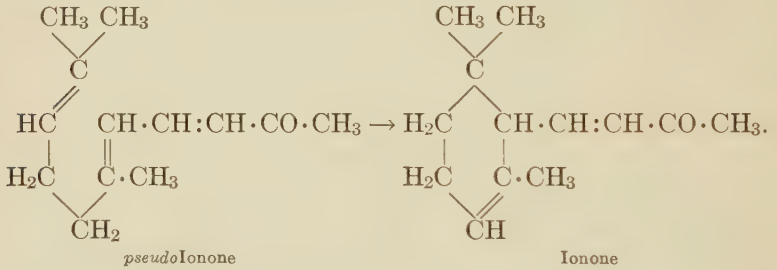
$$(CH_3)_2C{=}CH\cdot CH_2\cdot CH_2\cdot C(CH_3){=}CH\cdot CHO + H_2CH\cdot CO\cdot CH_3 =$$

(Geranial; Acetone)

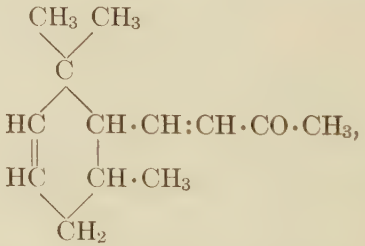
$$= H_2O + (CH_3)_2C{=}CH\cdot CH_2\cdot CH_2\cdot C(CH_3){=}CH\cdot CH{=}CH\cdot CO\cdot CH_3.$$

(*pseudo*Ionone)

*pseudo*Ionone is transformed into *ionone* by boiling with dilute sulphuric acid:



The structure of ionone is proved by its decomposition-products. It is manufactured as an artificial perfume, having a powerful violet-like odour, and being related closely to *irone*, the active principle of violets. The formula of irone is



and differs from that of ionone only in the position occupied by the double bond in the carbon ring.

COMPOUNDS WITH MORE THAN ONE SUBSTITUENT.

I. HALOGEN DERIVATIVES OF METHANE.

144. The halogen derivatives of the saturated hydrocarbons obtained by replacement of a single hydrogen atom by halogen are termed alkyl halides, and are described in **52–53**. This chapter treats of the compounds formed by exchange of more than one hydrogen atom for halogen.

It is possible to replace in successive stages the four hydrogen atoms in methane by the direct action of chlorine or bromine in presence of sunlight. Iodine does not react with methane or its homologues, but the action of fluorine is very energetic and effects complete substitution.

In practice, direct halogenation is not adopted for the preparation of the compounds CH_2X_2, CHX_3, or CX_4. They are obtained from the trihalogen derivatives prepared readily by another method, and convertible by chlorination or bromination into tetrachloromethane or tetrabromomethane. Reduction of the trihalogenmethanes yields dihalogenmethanes. On account of their important therapeutic properties, the compounds CHX_3 are prepared on the large scale.

Trichloromethane or Chloroform, $CHCl_3$.

145. *Chloroform* is obtained in the laboratory by distilling alcohol with bleaching-powder, acetone being employed on the manufacturing scale. This reaction involves simultaneous oxidation and chlorination, and acetaldehyde is assumed to be produced first by oxidation of the alcohol, and then to be transformed into *trichloroacetaldehyde* or *chloral*, $CCl_3 \cdot CHO$. This substance is converted by bases into chloroform and formic acid (**201**), in this instance by the slaked lime present in the bleaching-powder.

Chloroform is a liquid boiling at 61°, and solidifying at −70°. At 15° its density is 1·498. It is very slightly soluble in water, and possesses a characteristic ethereal odour and sweet taste. In 1847 Simpson

discovered that its prolonged inhalation produces unconsciousness, the basis of its value as an anæsthetic in surgical operations.

> Its use for this purpose is not wholly free from danger. Notwithstanding the fund of experience accumulated through the frequency of its application, occasionally the inhalation of chloroform is attended by fatal results. Ordinary ether and ethyl chloride are less dangerous, do not produce such disagreeable after-effects, and hence latterly have been preferred as anæsthetics (**56**).

Chloroform is a somewhat unstable substance, decomposing under the influence of light and air into chlorine, hydrogen chloride, and carbonyl chloride, $COCl_2$. A considerable proportion of this oxychloride is produced by bringing chloroform-vapour into contact with a flame. Its suffocating effect renders it very dangerous. The decomposition of the liquid can be prevented almost completely by adding one per cent. of alcohol, and keeping the chloroform in bottles of non-actinic glass.

The halogen atoms of chloroform take part in double decompositions, sodium ethoxide yielding the ethyl ester of orthoformic acid:

$$CH\boxed{Cl_3+3Na}\cdot OC_2H_5=CH(OC_2H_5)_3+3NaCl.$$

Formic acid can be obtained by warming chloroform with dilute alkalis, orthoformic acid probably being formed first, although it has not been isolated. On contact of chloroform with a forty per cent. aqueous solution of potassium hydroxide, carbon monoxide is evolved, chloromethene, CCl_2, being assumed to be formed as an intermediate product.

When chloroform is warmed with alcoholic ammonia and potassium hydroxide, its three chlorine atoms are replaced by nitrogen with production of potassium cyanide. The formation of *iso*carbonitriles from chloroform, alcoholic potassium hydroxide, and primary amines, has been mentioned (**77**).

Exposure to dark electric discharge converts chloroform into a series of highly chlorinated products, such as C_2Cl_4, C_2HCl_5, C_2Cl_6, C_3HCl_7, and others of similar type.

> *Dichloromethane*, CH_2Cl_2, is obtained from chloroform by reduction with zinc and hydrogen chloride in alcoholic solution. It is a liquid, boils at 40°, and has the density 1·337.
>
> *Tetrachloromethane* or *carbon tetrachloride*, CCl_4, produced by the action of chlorine on chloroform or carbon disulphide, is also a liquid, and boils at 76°. When heated with excess of water at 250° it yields hydrogen chloride

and carbon dioxide. At 20° its density is 1·593, the high densities of these polychloro-compounds being noteworthy. The bromine and iodine compounds are much denser than the corresponding chlorine compounds.

Tribromomethane or *bromoform*, $CHBr_3$, is obtained by methods analogous to those employed in the preparation of chloroform. It melts at 7·8°, boils at 151°, and at 15° has the density 2·904. It is utilized for therapeutic purposes.

Tri-iodomethane or Iodoform, CHI_3.

146. *Iodoform* is a substance of great importance, and is prepared from alcohol by the action of potassium carbonate and iodine. The intermediate product *iodal*, $CI_3 \cdot CHO$, analogous to chloral, has not been isolated. Being less expensive than alcohol, acetone often is employed on the manufacturing scale.

Iodoform can be prepared also by the electrolysis of a solution containing 60 g. of potassium iodide, 20 g. of sodium carbonate, and 80 c.c. of alcohol per 400 c.c., the temperature being kept between 60° and 65°. Iodine is liberated at the anode, so that the alcohol, potassium carbonate, and iodine necessary to the formation of iodoform are present in the mixture. By this method about eighty per cent. of the potassium iodide is converted into iodoform, the remainder of the iodine being obtained as potassium iodate. The formation of iodate can be avoided to a great extent by surrounding with parchment the cathode, where potassium hydroxide is formed. This procedure prevents contact of the potassium carbonate with the iodine set free at the anode.

Iodoform is a solid, and crystallizes in yellow hexagonal plates, well-developed crystals about a centimètre in length being obtained by the slow evaporation of a solution in anhydrous acetone. It has a peculiar saffron-like odour, sublimes very readily, and melts at 119°.

These characteristic properties of iodoform make its formation an important test for alcohol, although acetaldehyde, acetone, and several other substances similarly yield iodoform. Compounds containing the group $CH_3 \cdot C\equiv$ in union with oxygen answer the *iodoform-test*. It involves addition of iodine to the liquid under examination, and then potassium-hydroxide solution drop by drop until the colour of the iodine vanishes. With a considerable proportion of alcohol a yellow precipitate forms at once; with traces, the precipitate separates after a time. The reaction is sufficiently delicate to detect traces of alcohol in a sample of well-water or rain-water, after concentration by repeated distillation, the first fraction in each operation being collected.

Iodoform is employed in surgery as an antiseptic, but does not kill the bacteria directly. Its action on the micro-organisms requires a preliminary

decomposition, effected under the influence of the heat of the body by fermentation induced by the matter exuded from the wound.

Di-iodomethane, CH_2I_2, is a liquid, and is obtained by the reduction of iodoform with hydrogen iodide, phosphorus being added to regenerate the hydrogen iodide. At 18° its density is 3·292, a remarkably high value.

II. HALOGEN DERIVATIVES OF THE HOMOLOGUES OF METHANE.

147. Obviously the halogen derivatives of the homologues of methane present numerous examples of isomerism. Replacement by chlorine of three hydrogen atoms in normal pentane may yield several different compounds: a methyl-group may be converted into CCl_3; two chlorine atoms may replace the hydrogen of one methylene-group, and the third another hydrogen atom in the molecule; or the three chlorine atoms may unite with different carbon atoms; and so on.

The preparation of many of the halogen compounds included under this heading has been described already, the compounds $C_nH_{2n+1}\cdot CHX_2$ being obtained by the action of phosphorus pentahalide on aldehydes, and the derivatives $C_pH_{2p+1}\cdot CX_2\cdot C_qH_{2q+1}$ from ketones by a similar method (**98**). Compounds with two halogen atoms attached to two adjoining carbon atoms are formed by addition of halogen to the hydrocarbons C_nH_{2n}; those having four halogen atoms, two being united directly to each of two adjoining carbon atoms, are produced by addition of halogen to hydrocarbons with a triple bond; compounds of the type $C_pH_{2p+1}\cdot CHX\cdot CHX\cdot C_rH_{2r}\cdot CHX\cdot CHX\cdot C_mH_{2m+1}$ are obtained by addition of halogen to the hydrocarbons C_nH_{2n-4} with two double bonds; etc.

A method for the preparation of compounds rich in halogen from the saturated hydrocarbons is the exchange of one hydrogen atom for halogen, elimination of hydrogen halide by means of alcoholic potash, halogenation of the hydrocarbon C_nH_{2n} thus obtained, removal of one molecule of hydrogen halide, renewed halogenation of the product, and so on:

$$\underset{\text{Ethane}}{CH_3\cdot CH_3} \rightarrow \underset{\text{Ethyl chloride}}{CH_3\cdot CH_2Cl} - HCl \rightarrow \underset{\text{Ethylene}}{CH_2{:}CH_2} + 2Cl \rightarrow$$

$$\rightarrow \underset{\text{Ethylene chloride}}{CH_2Cl\cdot CH_2Cl} - 2HCl \rightarrow \underset{\text{Acetylene}}{CH{\equiv}CH} + 4Cl \rightarrow$$

$$\rightarrow \underset{\text{Tetrachloroethane}}{CHCl_2\cdot CHCl_2} - HCl \rightarrow \underset{\text{Trichloroethylene}}{CHCl{:}CCl_2} + 2Cl \rightarrow$$

$$\rightarrow \underset{\text{Pentachloroethane}}{CHCl_2\cdot CCl_3} - HCl \rightarrow \underset{\text{Tetrachloroethylene}}{CCl_2{:}CCl_2} + 2Cl \rightarrow \underset{\text{Hexachloroethane}}{CCl_3\cdot CCl_3}.$$

Another mode of producing polybromo-compounds involves the direct action of bromine on the hydrocarbons of the series C_nH_{2n+2} in presence of a small proportion of anhydrous iron bromide or iron-wire.

The course of this reaction is determined by the following factors:

1. At a temperature below 100°, with or without a catalyst, a molecule having n carbon atoms can take up $n-1$ atoms of halogen, these atoms becoming attached to the carbon atoms lacking halogen.

2. When $n-1$ halogen atoms are united already, a succeeding atom becomes attached to either the halogen-free carbon atom or the carbon atom with most hydrogen atoms.

3. The union of further halogen atoms is chiefly with the carbon atoms carrying most hydrogen atoms.

Individual Members.

148. Only a few of the numerous compounds of this group will be described.

1:1:2:2-*Tetrachloroethane*, $CHCl_2 \cdot CHCl_2$, is prepared technically by the interaction of chlorine and acetylene with antimony pentachloride as catalyst. It is a liquid boiling at 147°. Heating with milk of lime eliminates hydrogen chloride and forms 1:1:2-*trichloroethene*, $CCl_2:CHCl$, a liquid boiling at 88°. On addition of zinc-dust to an aqueous suspension of tetrachloroethane, heat is developed, and pure 1:2-*dichloroethene*, CHCl:CHCl, distils. It is a liquid boiling at 55°. Each of these substances is an excellent solvent for fats and oils; and each dissolves sulphur readily, being employed in vulcanizing caoutchouc.

Ethylene chloride or 1:2-*dichloroethane*, $CH_2Cl \cdot CH_2Cl$, is termed "Dutch Liquid," or the "Oil of the Dutch Chemists," it having been prepared first at the end of the eighteenth century by four Dutch chemists, Deiman, Bondt, Paets van Troostwyk, and Lauwerenburgh, by the action of chlorine on ethylene. It is a liquid boiling at 84·9°, and at 0° has the density 1·28.

Hexachloroethane, C_2Cl_6, is formed by the direct union of carbon and chlorine under the influence of a powerful arc-discharge between carbon poles in an atmosphere of chlorine.

Ethylene bromide or 1:2-*dibromoethane* is employed for syntheses and as a solvent. It is prepared by passing ethylene into bromine covered with a layer of water to prevent evaporation, the addition taking place very readily. Ethylene bromide is a colourless liquid of agreeable odour, solidifies at 8°, boils at 131°, and at 15° has the density 2·189.

Trimethylene bromide or 1:3-*dibromopropane*, $CH_2Br \cdot CH_2 \cdot CH_2Br$, also plays an important part in syntheses, and is obtained by addition of

hydrogen bromide to allyl bromide, $CH_2{:}CH{\cdot}CH_2Br$, produced from allyl alcohol. This method of formation suggests the constitution $CH_3{\cdot}CHBr{\cdot}CH_2Br$, that of the addition-product obtained by the action of bromine on propene, $CH_3{\cdot}CH{:}CH_2$. The two compounds not being identical, trimethylene bromide must have the 1:3-formula. It is a liquid boiling at 165°, and at 17° has the density 1·974.

Pentamethylene dibromide or 1:5-*dibromopentane* has the constitution indicated by the formula $CH_2Br{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br$.

III. POLYHYDRIC ALCOHOLS.

149. With more than one hydrogen atom of a saturated hydrocarbon replaced by hydroxyl, it is possible theoretically to have more than one hydroxyl-group in union with a single carbon atom, or to have each attached to a different one. It should be possible to obtain compounds of the first class by replacement of halogen by hydroxyl in the halogen derivatives $R{\cdot}CHX_2$, $R{\cdot}CX_3$, and $R{\cdot}CX_2{\cdot}R'$. Silver acetate converts halogen compounds of this type into stable acetates, such as $CH_2{<}\begin{matrix}OC_2H_3O\\OC_2H_3O\end{matrix}$. Saponification does not yield dihydric alcohols like $CH_2(OH)_2$, but gives aldehydes by elimination of one molecule of water. Sodium ethoxide converts compounds of the type $RCCl_3$ into *ortho-esters* with the general formula $R{\cdot}C(OC_2H_5)_3$. Saponification of these substances does not produce $R{\cdot}C(OH)_3$, the corresponding acid being formed instead through loss of water. Ethers of dihydric alcohols, such as $CH_3{\cdot}CH{<}\begin{matrix}OC_2H_5\\OC_2H_5\end{matrix}$, are known, and are termed *acetals* (104, 2). Their hydrolysis does not yield $R{\cdot}CH(OH)_2$, but an aldehyde. *These facts indicate compounds with more than one hydroxyl-group attached to the same carbon atom to be unstable*, although sometimes it is possible to obtain such derivatives (127, 201, 204, 230, and 234).

Many substances containing several hydroxyl-groups are known, not more than one hydroxyl being in union with each carbon atom.

3. Alkanediols or Glycols.

150. The *glycols* are obtained from the corresponding halogen compounds analogously to the monohydric alcohols (39).

The exchange of halogen for hydroxyl can be caused by means of acetate of silver or the acetate of an alkali-metal, and saponification of the diacetate obtained. It also can be effected directly by boiling with sodium-carbonate solution, or with water and lead oxide.

Glycols of the type R·CHOH·CHOH·R, with the CHOH-groups in direct union, are formed from alkenes either through the medium of their bromine addition-products, or by the direct addition of two hydroxyl-groups by means of careful oxidation with potassium permanganate. Ethene yields the simplest dihydric alcohol, *glycol*:

$$CH_2{:}CH_2+H_2O+O=CH_2OH\cdot CH_2OH.$$

Another method for the formation of glycols of this type consists in the reduction of ketones, either by sodium in aqueous solution or by electrolysis. Acetone yields *pinacol* and *iso*propyl alcohol. Glycols of the type of pinacol are termed *pinacols*, and can be obtained without admixture of a secondary alcohol by reduction of aldehydes or ketones with magnesium-amalgam, an initial addition-product being formed with evolution of heat:

$$2CH_3\cdot C{}^{H}_{O}+Mg=\begin{array}{c}CH_3\cdot CH\text{——}CH\cdot CH_3\\ \dot{O}\cdot Mg\cdot \dot{O}\end{array};$$

$$\text{or}\quad 2CH_3\cdot CO\cdot CH_3+Mg=\begin{array}{c}{}^{CH_3}_{CH_3}{>}C\text{——}C{<}^{CH_3}_{CH_3}\\ |\qquad\quad |\\ O\cdot Mg\cdot O\end{array}.$$

Water decomposes the addition-product, with formation of the pinacol:

$$\begin{array}{c}{}^{CH_3}_{CH_3}{>}C\text{——}C{<}^{CH_3}_{CH_3}\\ |\qquad\quad |\\ O\cdot Mg\cdot O\end{array}+2H_2O={}^{CH_3}_{CH_3}{>}C(OH)\text{—}C\begin{cases}CH_3\\(OH)\\CH_3\end{cases}+MgO.$$

The constitution of pinacol is indicated by its synthesis:

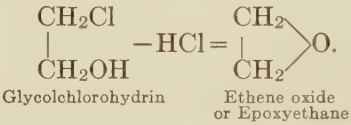
$$\begin{array}{c}CH_3\cdot CO\cdot CH_3+H\\ \\ CH_3\cdot CO\cdot CH_3+H\\ \text{Acetone}\end{array}=\begin{array}{c}CH_3\cdot C(OH)\cdot CH_3\\ |\\ CH_3\cdot C(OH)\cdot CH_3\\ \text{Pinacol}\end{array}.$$

Distillation with dilute sulphuric acid induces in pinacol a remarkable intramolecular transformation, explicable on the assumption of a hydroxyl-group having changed place with a methyl-group:

$$\underset{\text{Pinacol}}{(CH_3)_2C(OH)\cdot C}\begin{cases}OH\\CH_3\\CH_3\end{cases}\rightarrow (CH_3)_3C\cdot C\begin{cases}O|H\\ \boxed{OH}\\CH_3\end{cases}-H_2O=\underset{\text{Pinacolin}}{(CH_3)_3C\cdot CO\cdot CH_3}.$$

The constitution of *pinacolin* can be inferred from its synthesis by the action of zinc methide on trimethylacetyl chloride, $(CH_3)_3C\cdot COCl$, and in other ways.

Most of the glycols are colourless viscous liquids of sweet taste, the origin of the name of the series. Their boiling-points and densities are considerably higher than those of the monohydric alcohols with the same number of carbon atoms. Glycol boils at 197·5°, and ethyl alcohol at 78°; at 0° the density of glycol is 1·128, and of ethyl alcohol 0·806. The nature of the hydroxyl-groups in glycol and that in the monohydric alcohols is perfectly analogous; since exchange of hydroxyl for halogen, the formation of ethers, esters, and alkoxides, and the oxidation of primary glycols to aldehydes and acids, may occur in connexion with one or both of the hydroxyl-groups. For instance, compounds such as $CH_2OH \cdot CH_2Cl$, *glycolchlorohydrin*; $CH_2OC_2H_5 \cdot CH_2OH$, *glycolmonoethyl ether*; and $CH_2OC_2H_5 \cdot CH_2OC_2H_5$, *glycol diethyl ether* are known. The glycols possess a property due to the presence of two hydroxyl-groups, the power of forming anhydrides. The first member of the series, glycol, $CH_2OH \cdot CH_2OH$, does not yield an anhydride by the direct elimination of water, but a compound of the formula C_2H_4O is obtained by first replacing one hydroxyl-group by an atom of chlorine and then eliminating hydrogen chloride:



Glycolchlorohydrin — Ethene oxide or Epoxyethane

Epoxyethane or *ethene oxide* boils at 14° and normally is gaseous. It takes up water readily, forming glycol; or hydrogen chloride, forming glycolchlorohydrin. To ethene oxide is assigned the constitutional formula indicated, because with phosphorus pentachloride it yields ethene chloride, the oxygen atom being replaced by two chlorine atoms. A compound with the possible but less probable (131) constitution $\begin{matrix} CH_2 \\ \| \\ CHOH \end{matrix}$ would not yield ethene chloride with this reagent.

Some of the higher homologues of glycol with a chain of four or five carbon atoms between the hydroxyl-groups produce anhydrides with a constitution analogous to that of ethene oxide. They show a marked diminution in the power of forming addition-products with water, the *closed chain* of carbon atoms and one oxygen atom being more stable than that in ethene oxide.

2. Trihydric Alcohols.

151. The principal representative of the group of trihydric alcohols is *glycerol* or "glycerine," $C_3H_5(OH)_3$, discovered by Scheele in 1779.

The technical process available for the production of this substance is more than a century old, and involves the saponification of fats and oils, the glyceryl esters of the higher fatty acids (85 and 155). During the war of 1914 to 1918, glycerol was manufactured by the fermentation of sugars in presence of sodium sulphite (221), but this method has been abandoned.

The synthesis of glycerol was effected in 1873 by Friedel and Silva, their basis being acetic acid. This acid can be synthesized from its elements in various ways, an example being the oxidation of acetaldehyde formed by the action of water on acetylene (125). Dry distillation of calcium acetate yields acetone, convertible by reduction into *iso*propyl alcohol. Elimination of the elements of water from this alcohol generates propene, a hydrocarbon transformed by chlorine into 1:2-dichloropropane, this substance being converted by means of iodine chloride into trichlorohydrin. When heated with water at 170°, trichlorohydrin yields glycerol:

$$\underset{\text{Acetic acid}}{CH_3\cdot COOH} \rightarrow \underset{\text{Acetone}}{CH_3\cdot CO\cdot CH_3} \rightarrow \underset{\text{\textit{iso}Propyl alcohol}}{CH_3\cdot CHOH\cdot CH_3} \rightarrow \underset{\text{Propene}}{CH_3\cdot CH{:}CH_2} \rightarrow$$

$$\rightarrow \underset{\text{1 : 2-Dichloropropane}}{CH_3\cdot CHCl\cdot CH_2Cl} \rightarrow \underset{\text{Trichlorohydrin}}{CH_2Cl\cdot CHCl\cdot CH_2Cl} \rightarrow \underset{\text{Glycerol}}{CH_2OH\cdot CHOH\cdot CH_2OH}.$$

In accordance with the general rule respecting the inability of a carbon atom to unite with two hydroxyl-groups, glycerol can have only the structure $CH_2OH\cdot CHOH\cdot CH_2OH$. This constitution is supported by Friedel and Silva's synthesis and by other evidence:

1. Careful oxidation of allyl alcohol by means of potassium permanganate adds two hydroxyl-groups at the double bond:

$$CH_2{:}CH\cdot CH_2OH \rightarrow CH_2OH\cdot CHOH\cdot CH_2OH.$$

2. *Glyceric acid*, $C_3H_6O_4$, is the product of the careful oxidation of glycerol, $C_3H_8O_3$, a reaction corresponding with the formation of acetic acid, $C_2H_4O_2$, from ethanol, C_2H_6O, by exchange of two hydrogen atoms for one oxygen atom, and indicating glycerol to contain one —CH_2OH-group. Further oxidation converts glyceric acid into *tartronic acid*, $C_3H_4O_5$, two hydrogen atoms being replaced by one oxygen atom with formation of a new carboxyl-group. Glycerol therefore contains two —CH_2OH-groups in the molecule, its constitution being $CH_2OH\cdot CH_2O\cdot CH_2OH$. Since tartronic acid, $COOH\cdot CH_2O\cdot COOH$, still possesses alcoholic properties, the group CH_2O must have the constitution $>CHOH$. It must be similar in the molecule of glycerol, proving the structure of this alcohol to be $CH_2OH\cdot CHOH\cdot CH_2OH$.

3. A further proof of the constitution indicated is the formation of glycerol from 1:2:3-tribromopropane or tribromohydrin (147).

152. Glycerol is a colourless oily liquid of sweet taste. It is very hygroscopic, and is miscible in all proportions with water and alcohol, but is insoluble in ether. Exposure for some time to a low temperature causes solidification, but the crystals formed do not melt below 17°. It boils at 290°, and at 15° has the density 1·265. Its chemical behaviour accords completely with the constitution of a trihydric alcohol, exemplified by its yielding three esters by replacement of one, two, or three hydroxyl-groups. When borax is dissolved in glycerol or in a solution of it and the mixture is introduced into the flame, the green colour characteristic of free boric acid is observed, this reaction constituting the basis of SENIER's test for glycerol. Blood contains a small proportion of glycerol.

The production of *acraldehyde* (141) by the elimination of water from glycerol can be represented by the scheme

$$\begin{array}{c} \boxed{\dot{O}HH} \\ CH_2\cdot\dot{C}\text{—}\dot{C}HOH. \\ \boxed{\dot{O}H\ \dot{H}} \end{array}$$

$CH_2{:}C{:}CHOH$ should be obtained, but changes immediately to acraldehyde, $CH_2{:}CH\cdot C\begin{smallmatrix}H\\O\end{smallmatrix}$ (131).

153. Glycerol is employed extensively in the arts and in medicine. One of its most important applications is to the preparation of the so-called "Nitroglycerine." This explosive has a misleading name, being *glyceryl trinitrate*,

$$\begin{array}{l} CH_2O\cdot NO_2 \\ \dot{C}HO\cdot NO_2, \\ \dot{C}H_2O\cdot NO_2 \end{array}$$

and not a nitro-compound (68), for its saponification with alkalis yields glycerol and the nitrate of the corresponding alkali-metal.

Glyceryl trinitrate is prepared by bringing glycerol into contact with a mixture of concentrated sulphuric acid and nitric acid, rise of temperature being prevented. Other polyhydric alcohols are converted analogously into nitrates. After a time, the reaction-mixture is poured into water, the nitrate separating in the form of an oily, very explosive liquid of faint, headache-producing odour. It can be purified by washing with water, the pure product not exploding spontaneously.

The density of glyceryl trinitrate is 1·6. Its metastable form solidifies at 2·2°, and its stable modification at 12·2°.

154. Glyceryl trinitrate is a liquid, and its use in that form for technical purposes being attended with difficulties, it is mixed with infusorial earth ("Kieselguhr"), being absorbed to form a soft plastic mass, *dynamite*, containing usually 75 per cent. of the trinitrate and 25 per cent. of the earth. Glyceryl trinitrate can be obtained in the solid form also by dissolving in it a small proportion of guncotton (228) to convert it into an elastic solid termed "Blasting gelatine," and resembling jujubes in consistence. This substance has the advantage over dynamite of not leaving any solid residue after explosion. Dynamite cannot be employed as ammunition, its velocity of explosion being so great as to produce an impulse too violent for a gun to resist without bursting. In technical language it is said to exert a "Brisant" or detonating effect.

155. *Fats and oils.*—Large quantities of these substances exist in both the animal kingdom and the vegetable kingdom. In them the three hydroxyl-groups of glycerol have been esterified by higher fatty acids. The *hard fats* such as beef-tallow and mutton-tallow are derived almost exclusively from palmitic acid and stearic acid. The *soft fats* also are derived from these acids in conjunction with unsaturated acids such as oleic acid, and are exemplified by lard and palm-kernel fat.

In contrast with the essential oils (363), which are volatile with steam, the *fatty* or *fixed oils* are glyceryl triesters of unsaturated acids. Two types are recognized, the *non-drying oils* and the *drying oils*. The first type includes *olive oil* and *almond oil*, the main product of their saponification being oleic acid. The name "drying oils" originated in the property characteristic of these substances of being transformed by atmospheric oxygen into a hard transparent product, as a result of which they find wide application in the varnish industry. They are derived from higher fatty acids with two double bonds, such as linoleic acid from linseed oil.

Butter occupies a unique position among the fats, being derived by the esterification with glycerol of a mixture of *volatile fatty acids* and two of their higher homologues, stearic acid and palmitic acid.

When butter is saponified with potassium hydroxide, the fatty acids are converted into potassium salts. On addition of dilute sulphuric acid to these salts and subsequent distillation, *n*-butyric acid distils with the steam, being accompanied by other fatty acids, such as caproic acid, in small proportion. The name "volatile fatty acids" originated from this property. Since these acids are not obtained by similar treatment of other animal fats or of vegetable fats, their presence furnishes the most important test between butter and margarine. Owing to the proportion of volatile fatty acids in butter not being constant, but varying within wide limits, their estimation alone usually is insufficient to determine whether the

butter is pure or has been adulterated with margarine. Other tests must be applied, such as a determination of the refraction of the molten fat, that of butter having a value lower than that of margarine.

The natural fats are always mixtures of various tri-esters of glycerol, the esterification of the three hydroxyl-groups of that substance having been effected normally not by a single fatty acid but by different members of the series. It is, however, possible to synthesize bodies which are tri-esters of glycerol, and therefore simple fats, by heating the two substances in the molecular proportion 1 : 3 at 200° under reduced pressure until the liberation of water ceases.

The fats play a significant part in the nutriment of the human race and of animals, and are a most important constituent of food. During digestion, the fats are hydrolyzed by the action of the enzyme *lipase* secreted by the pancreatic glands, the glycerol and fatty acids produced recombining in the body to yield fats anew.

The fat industry is very extensive, and includes such branches as the manufacture of soap (85), that of "stearine" candles (85), and that of margarine. The main feature of margarine production is the mixing of purified hard fats with soft fats or oils in such proportion as to yield a substance with the consistence of butter.

Since the very large quantities of solid fats consumed in the margarine industry now exceed the supplies available, whilst much greater amounts of oils are being produced, a process for "hardening" oils or converting them into solid fats has acquired very marked technical importance. It depends on the ready combination of hydrogen with the unsaturated acids to form saturated acids, effected by passing a current of the gas at a pressure exceeding one atmosphere through a continuously agitated mixture of the oil and powdered nickel at a temperature of approximately 200°.

3. Tetrahydric and Other Polyhydric Alcohols.

156. Among the tetrahydric alcohols is the natural product *erythritol*, $CH_2OH \cdot CHOH \cdot CHOH \cdot CH_2OH$. It contains a normal carbon chain, because reduction with hydrogen iodide converts it into 2-*iodobutane*, $CH_3 \cdot CHI \cdot CH_2 \cdot CH_3$.

Examples of pentahydric alcohols are *arabitol* and *xylitol*, $C_5H_{12}O_5$. They are stereoisomerides, as are also the hexahydric alcohols *dulcitol* and *mannitol*, $C_6H_{14}O_6$, both found in nature. Each has a normal carbon chain, and resembles erythritol in yielding a *n*-secondary iodide on reduction with hydrogen iodide, mannitol being converted into 3-*iodohexane*,

$$CH_3 \cdot CH_2 \cdot CHI \cdot CH_2 \cdot CH_2 \cdot CH_3.$$

They can be obtained artificially by the reduction of the corresponding aldehydes or ketones, dulcitol being formed from galactose, and mannitol from mannose and lævulose. The reason for assuming their stereoisomerism is explained in **205**, but here may be noted the presence in the polyhydric alcohols of asymmetric carbon atoms, indicated in the formulæ by asterisks:

$$CH_2OH \cdot \overset{*}{C}HOH \cdot CHOH \cdot \overset{*}{C}HOH \cdot CH_2OH;$$

Arabitol and Xylitol

$$CH_2OH \cdot \overset{*}{C}HOH \cdot \overset{*}{C}HOH \cdot \overset{*}{C}HOH \cdot \overset{*}{C}HOH \cdot CH_2OH.$$

Dulcitol and Mannitol

157. The polyhydric alcohols prevent the precipitation of the hydroxides of copper, iron, and other metals by means of alkalis, a solution of cupric sulphate and glycerol not yielding a precipitate of cupric hydroxide with potassium hydroxide. This phenomenon is due to the formation of soluble metallic compounds of the polyhydric alcohols, the hydroxyl-hydrogen being replaced by the metal. The acidic nature of the hydroxyl-group, a characteristic almost lacking in the monohydric alcohols, is developed therefore in some measure by increase in the number of these groups present in the molecule. This property is possessed not only by the polyhydric alcohols, but also by many other compounds containing several hydroxyl-groups (**191**).

IV. DERIVATIVES CONTAINING HALOGEN ATOMS, HYDROXYL-GROUPS, NITRO-GROUPS, OR AMINO-GROUPS.

158. Only a few of the numerous compounds belonging to this class will be considered. The chemical properties of its members are determined by the substituents.

Substances with halogen and hydroxyl in union with the same carbon atom are not known; but derivatives having these substituents attached to different carbon atoms are obtained from the polyhydric alcohols by partial exchange of hydroxyl for halogen, and have the general name *halogen-hydrins*. *Glycerol dichlorohydrin*, $C_3H_5(OH)Cl_2$, is formed by saturating with hydrogen chloride a solution of glycerol in glacial acetic acid. It has the symmetrical formula $CH_2Cl \cdot CHOH \cdot CH_2Cl$, for it differs from the dichlorohydrin obtained by addition of chlorine to allyl alcohol, this derivative having the constitution $CH_2OH \cdot CHCl \cdot CH_2Cl$. Each dichlorohydrin is converted by potassium hydroxide into *epichlorohydrin*,

$$\begin{array}{l} CH_2 \cdot CH \cdot CH_2Cl \\ \quad\;\; \diagdown\!\diagup \\ \quad\;\; O \end{array} .$$

Dinitro-compounds having both nitro-groups in union with the same carbon atom are formed from primary bromo-nitro-compounds by the action of potassium nitrite:

$$CH_3 \cdot CHBrNO_2 + KNO_2 = CH_3 \cdot CH(NO_2)_2 + KBr.$$

The hydrogen atom belonging to the carbon atom carrying the nitro-groups can be replaced readily by metals, an indication of the acidic character of these primary dinitro-compounds (322).

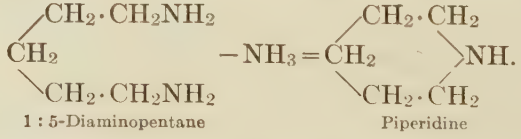
159. *Diamines* with the two amino-groups attached to the same carbon atom are not numerous, most of them having their amino-groups in union with different carbon atoms. Some of these compounds are formed by the putrefaction of animal matter such as flesh, and are classed as *ptomaines* with other basic substances similarly formed. Such are *cadaverine* or 1:5-*diaminopentane*,

$$NH_2 \cdot CH_2 \cdot (CH_2)_3 \cdot CH_2 \cdot NH_2,$$

and *putrescine* or 1:4-*diaminobutane*, $NH_2 \cdot CH_2 \cdot (CH_2)_2 \cdot CH_2 \cdot NH_2$. The constitution of these substances has been proved by synthesis, 1:5-diaminopentane having been obtained from 1:3-dibromopropane, $Br \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot Br$. This substance is converted by potassium cyanide into propane-1:3-dicarbonitrile, $CN \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CN$, reduction with sodium and boiling alcohol transforming the cyano-groups of this product into CH_2NH_2-groups (78), with formation of the diamine:

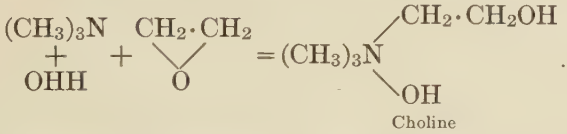
$$\begin{matrix} CN \\ | \\ (CH_2)_3 \\ | \\ CN \end{matrix} \rightarrow \begin{matrix} CH_2NH_2 \\ | \\ (CH_2)_3 \\ | \\ CH_2NH_2 \end{matrix} .$$

Heating 1:5-diaminopentane hydrochloride eliminates one molecule of ammonia from each molecule, and converts it into *piperidine* with the character of a saturated secondary amine. For this reason and other reasons (388) piperidine is assigned a ring or cyclic formula:



When heated, 1:4-diaminobutane and 1:3-diaminopropane yield analogous cyclic compounds, but less readily, whereas diaminoethane does not.

160. *Choline*, $C_5H_{15}O_2N$, is partly amine and partly alcohol, and should be mentioned on account of its physiological importance. It is distributed widely throughout both the animal world and the vegetable kingdom. Its constitution is inferred from its synthesis by the interaction of trimethylamine and ethene oxide in aqueous solution:



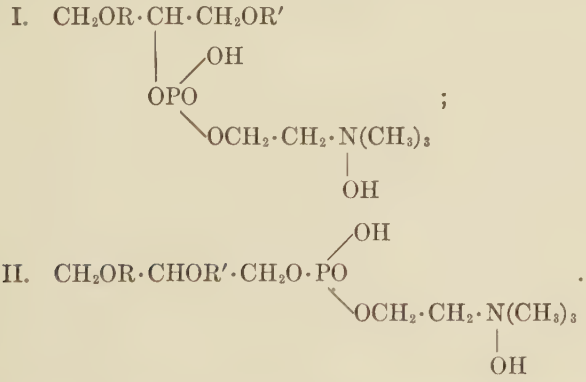
Choline

A derivative widely distributed throughout both the natural kingdoms, and closely related to choline, is *colamine* or aminoethyl alcohol, $NH_2 \cdot CH_2 \cdot CH_2OH$ (349).

Choline and colamine are constituents of very complex compounds known as *phosphatides* on account of their phosphorus content, and present in the spleen, the brain, yolk of egg, and elsewhere. The phosphatides are derivatives of glycerol with one or two of its hydroxyl-groups esterified by fatty acids, and of phosphoric acid in union with a basic substance.

The *lecithines* are derived from glycerophosphoric acid, and are the most important members of the phosphatide group.

With baryta-water *lecithine* yields choline, one or more of the fatty acids named, and glycerophosphoric acid; and therefore it should have formula I or formula II, R and R′ being acidic radicals:



Many types of lecithine are known, the differences between them being partly due to the phosphoric-acid radical being in union either with one of the terminal hydroxyl-groups of the glycerol or with its central hydroxyl-group. The type with the phosphoric-acid radical located at the central carbon atom of glycerol is much the more common form. Another cause of difference is the nature of the acidic radicals united with both the other hydroxyl-groups to form esters.

The lecithines are optically active. In formula II the centre carbon atom of the glycerol residue is asymmetric. When the phosphoric-acid radical is united with the central carbon atom as in formula I, this atom can be asymmetric only if R and R′ be dissimilar, as in

$$CH_2OR \cdot CHOPh \cdot CH_2OR',$$

where Ph represents the phosphoric-acid radical. Natural lecithine is always a mixture of the different types.

The lecithines dissolve readily in alcohol, but with difficulty in ether. With both acids and bases they form salts corresponding with the two structural formulæ I and II.

Another important phosphatide is *kephaline*, present in the brain. It differs from the lecithines in structure through having aminoethanol or colamine as its basic constituent instead of choline.

Lecithines can be synthesized by the action of phosphoric oxide on such a substance as distearylglycerol, an ester of metaphosphoric acid and this acid itself being produced:

$$(CH_2OR)_2CHOH + O_2P \cdot OPO_2 \rightarrow (CH_2OR)_2CHO \cdot PO_2 + HPO_3.$$

Water transforms the metaphosphoric ester into the orthophosphoric ester, a substance convertible by choline into lecithine or by colamine into kephaline.

POLYBASIC ACIDS.

I. SATURATED DIBASIC ACIDS, $C_nH_{2n-2}O_4$.

161. Many isomerides of the acids $C_nH_{2n}(COOH)_2$ are possible theoretically, and differ from one another in the positions occupied by the carboxyl-groups in union with the carbon chain. For many reasons the most important are the $\alpha\alpha'$-acids (36) with carboxyl-groups attached to the terminal carbon atoms of the normal chain.

The general methods for the preparation of the dibasic acids and those for the monobasic acids are analogous. The dibasic acids are produced by the oxidation of the corresponding glycols and aldehydes, and by the hydrolysis of the dinitriles, although many of them are prepared by special methods.

Physical and Chemical Properties.

These acids are well-defined crystalline substances, and those with more than three carbon atoms can be distilled *in vacuo* without decomposition. When distilled at the ordinary pressure, many of them lose water.

The melting-points of these acids exhibit a peculiarity characteristic of the fatty acids (80), the members with an even number of carbon atoms having higher melting-points than those immediately succeeding them with an uneven number of carbon atoms, as is demonstrated by the table on next page.

This relation is represented graphically in Fig. 30, the melting-points of the even series and those of the uneven series approximating more and more closely as the number of the carbon atoms increases.

A similar peculiarity is characteristic of other physical constants of these acids, that of the solubility in water being given in the last column of the table. The solubility of the acids with an uneven number of carbon atoms is much greater than the solubility of those with an even number, and for both types the solubility diminishes with increase in the number of carbon atoms.

Verkade found alterations of this type to be associated only with properties characteristic of the solid state, and indicated the probability of such variations being connected with crystal form. He noted similar alternations for the heats of combustion of the solid dibasic acids, but not for those of their liquid dimethyl esters. Other physical properties of these liquids, such as boiling-point, refractivity, and density, do not exhibit the phenomenon.

Name.	Formula.	Melting-point.	Parts by Weight Soluble in 100 Parts of Water at 20°.
Oxalic acid	$COOH \cdot COOH$	189·5°*	8·6
Malonic acid	$COOH \cdot CH_2 \cdot COOH$	133°	73·5
Succinic acid	$COOH \cdot (CH_2)_2 \cdot COOH$	183°	5·8
Glutaric acid	$COOH \cdot (CH_2)_3 \cdot COOH$	97·5°	63·9
Adipic acid	$COOH \cdot (CH_2)_4 \cdot COOH$	153°	1·5
Pimelic acid	$COOH \cdot (CH_2)_5 \cdot COOH$	105·5°	5·0
Suberic acid	$COOH \cdot (CH_2)_6 \cdot COOH$	140°	0·16
Azelaic acid	$COOH \cdot (CH_2)_7 \cdot COOH$	108°	0·24
Sebacic acid	$COOH \cdot (CH_2)_8 \cdot COOH$	134·5°	0·10
Nonanedicarboxylic acid	$COOH \cdot (CH_2)_9 \cdot COOH$	110°	
Decamethylenedicarboxylic acid	$COOH \cdot (CH_2)_{10} \cdot COOH$	126°	
Brassylic acid	$COOH \cdot (CH_2)_{11} \cdot COOH$	112°	
Dodecamethylenedicarboxylic acid	$COOH \cdot (CH_2)_{12} \cdot COOH$	124°	

*Anhydrous oxalic acid.

Oxalic acid is a very much stronger acid than its homologues, as the dissociation-constants indicate. For oxalic acid 10^4k is about 1000, for

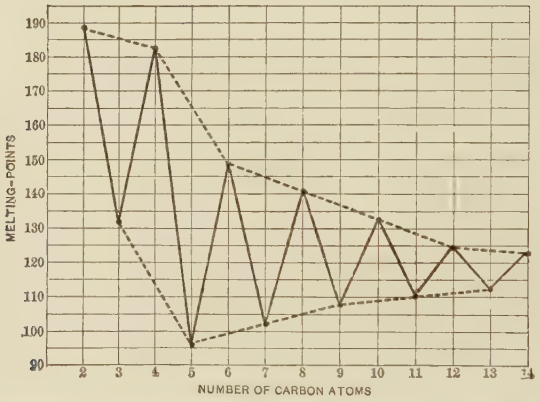


FIG. 30.—GRAPHIC REPRESENTATION OF THE MELTING-POINTS OF THE ACIDS $C_nH_{2n-2}O_4$.

malonic acid 16·3, and for succinic acid 0·65; for the remaining acids it has values diminishing with increase in the number of carbon atoms, but of the same order as the last number. The longer the carbon chain between the carboxyl-groups, the weaker is the acid (**172**). The values of the dissociation-constants are considerably higher than those of the corresponding saturated monobasic acids with the same number of carbon atoms.

Oxalic Acid, $C_2H_2O_4,2H_2O$.

162. Between *oxalic acid* and formic acid there exists a genetic interdependence, it being possible to prepare formic acid from oxalic acid, or conversely oxalic acid from formic acid. On heating potassium formate or sodium formate strongly, hydrogen is evolved from the fusing mass, and potassium oxalate or sodium oxalate is produced:

$$\begin{matrix} KOOC \\ KOOC \end{matrix}\Big|\begin{matrix} H \\ H \end{matrix}\Big| = \begin{matrix} KOOC \\ KOOC \end{matrix}\Big| + H_2.$$

The reverse transformation of oxalic acid into formic acid is described in 163, and constitutes the ordinary laboratory method for the preparation of formic acid.

Frequently oxalic acid is produced by the oxidation of organic substances with nitric acid, exemplified by its formation through the action of that acid on sugar. On the manufacturing scale it is prepared by heating to fusion a mixture of potassium hydroxide and sodium hydroxide along with sawdust. A formate is an intermediate product, and on further heating loses hydrogen, being converted into an oxalate. After cooling, the mass is lixiviated with water, the oxalate going into solution. The oxalic acid is precipitated as calcium oxalate by the addition of milk of lime, and obtained in the free state by the action of sulphuric acid.

The production of oxalic acid by the interaction of carbon dioxide and potassium or sodium in the neighborhood of 360°, and its formation by the hydrolysis of cyanogen, CN·CN, are of theoretical importance.

Oxalic acid occurs in nature in different plants, chiefly in species of *oxalis*, in the form of potassium hydrogen, or calcium, salt. Sometimes it is found in plant-cells as a crystalline deposit of calcium oxalate termed *raphides*. It crystallizes with two molecules of water of crystallization, and at 30° it begins to lose this water. On heating carefully the anhydrous acid sublimes, but when heated strongly, either alone or with concentrated sulphuric acid, it decomposes into carbon dioxide, carbon monoxide, and water. The velocity of this decomposition is dependent largely on small differences in the proportion of water present in the samples of concentrated acid employed, one of the few instances of a reaction being retarded by the influence of water. A similar decomposition ensues through exposure of a solution of uranium oxalate to sunlight, carbon monoxide and carbon dioxide being evolved energetically. Oxalic acid is oxidized very readily, a volumetric method for its estimation depending on the use of potassium permanganate in

sulphuric-acid solution, each molecule of oxalic acid requiring one atom of oxygen:

$$C_2H_2O_4+O=2CO_2+H_2O.$$

The oxidation with permanganate accords with the equation

$$2KMnO_4+5C_2H_2O_4+3H_2SO_4=K_2SO_4+2MnSO_4+10CO_2+8H_2O.$$

The manganese sulphate formed has a catalytic accelerating action on the process, the first few drops of permanganate solution being decolorized very slowly, but further addition of permanganate being attended by the instantaneous disappearance of the colour. When manganese sulphate is added to the oxalic-acid solution before the titration, the permanganate is decolorized at once.

Only the salts of the alkali-metals are soluble in water. Calcium oxalate, $CaC_2O_4,2H_2O$, is insoluble in acetic acid, but soluble in mineral acids; its formation serves as a test both for calcium and for oxalic acid. As a dibasic acid, oxalic acid yields both primary and normal salts. The so-called *quadroxalates* also are known, compounds of one molecule of primary salt with one molecule of acid, an example being "Salt of sorrel," $KHC_2O_4,H_2C_2O_4,2H_2O$. A great number of complex salts of oxalic acid is known, many of them containing alkali-metals, and being soluble in water. They are employed in electro-analysis.

A type of these complex salts is *potassium ferrous oxalate*, $K_2Fe(C_2O_4)_2$. It yields a yellow solution, indicating the presence of a complex ion, probably $(Fe(C_2O_4)_2)''$, ferrous salts being usually light-green. Potassium ferrous oxalate is a strong reducer, and is employed for the development of photographic plates.

Potassium ferric oxalate, $K_3Fe(C_2O_4)_3$, yields a green solution, denoting the presence of a complex ion, possibly $(Fe(C_2O_4)_3)'''$. Its solution is reduced rapidly by sunlight, in accordance with the equation

$$2K_3Fe(C_2O_4)_3=2K_2Fe(C_2O_4)_2+K_2C_2O_4+2CO_2.$$

This property is applied to the preparation of *platinotypes*. The photographic negative is placed on a sheet of paper saturated with potassium ferric oxalate, reduction to ferrous salt taking place only where the light is transmitted through the negative. On contact of the paper with a solution of a platinum salt, the metal is deposited only on the parts coated with potassium ferrous oxalate.

Eder's solution has remarkable properties. It consists of a mixture of two volumes of a four per cent. solution of ammonium oxalate, and one volume of a five per cent. solution of mercuric chloride. In the dark it remains unaltered, but under the influence of light it decomposes with precipitation of mercurous chloride:

$$2HgCl_2+(NH_4)_2C_2O_4=2HgCl+2CO_2+2NH_4Cl.$$

The decomposition is accelerated greatly by the presence of fluorescent substances such as eosin (348).

163. *Dimethyl oxalate* is a solid melting at 54°, and is employed in the preparation of pure methyl alcohol. *Diethyl oxalate* is a liquid. Each is prepared by distilling a solution of anhydrous oxalic acid in the absolute alcohol.

Oxalyl chloride, $COCl \cdot COCl$, is produced by the interaction of two gramme-molecules of phosphorus pentachloride and one gramme-molecule of oxalic acid. It is a colourless liquid, boils at 64°, and at −12° solidifies to white crystals. Contact of its vapour with steam forms oxalic acid and hydrochloric acid; but liquid water converts it quantitatively into carbon dioxide, carbon monoxide, and hydrochloric acid.

Oxamide, $CONH_2 \cdot CONH_2$, is a white solid nearly insoluble in water, alcohol, and ether, and is obtained as a crystalline precipitate by the addition of ammonia to a solution of a dialkyl oxalate. The monoamides of the dibasic acids are termed *amic acids*, that of oxalic acid being *oxamic acid*, $CONH_2 \cdot COOH$. It is a crystalline compound, readily soluble in cold water and insoluble in alcohol.

The interaction of oxalic acid, $HOOC \cdot COOH$, and glycerol yields either allyl alcohol (132) or formic acid (81), the product formed being dependent on the experimental conditions. This action constitutes the basis of the laboratory method of preparing each of these compounds.

On dissolving anhydrous oxalic acid in excess of glycerol at a temperature approximating to 50°, the initial product is an oxalic ester of glycerol (I), since addition of alcoholic ammonia produces oxamide as with other oxalic esters. Rise of temperature causes elimination of two molecules of carbon dioxide, with production of allyl alcohol (II):

$$\begin{array}{l} CH_2O \cdot CO \\ | \\ CHO - CO - 2CO_2 = \\ | \\ CH_2OH \\ \text{I.} \end{array} \qquad \begin{array}{l} CH_2 \\ \| \\ CH \\ | \\ CH_2OH \\ \text{II.} \end{array} \quad ; \quad \begin{array}{l} CH_2O \cdot CO \cdot CO_2H \\ | \\ CHOH \\ | \\ CH_2OH \\ \text{III.} \end{array} \qquad -CO_2 =$$

$$\begin{array}{l} CH_2O \cdot CO \cdot H + H_2O \\ | \\ = CHOH \\ | \\ CH_2OH \\ \text{IV.} \end{array} \qquad \begin{array}{l} CH_2OH \\ | \\ \rightarrow CHOH + H \cdot CO_2H. \\ | \\ CH_2OH \end{array}$$

The quantity of allyl alcohol formed is equivalent to that of the oxamide which can be precipitated from an equal volume of the reaction-mixture.

With oxalic acid containing water of crystallization, the initial product is the primary oxalic ester of glycerol (III). On warming, this compound readily loses one molecule of carbon dioxide, with formation of *glyceryl monoformate* or *monoformin* (IV). On adding more oxalic acid, formic acid is liberated and distils. Simultaneously, the primary oxalic ester of glycerol is formed again, and becomes available for the production of more formic acid. The glycerol is regenerated, indicating a given weight of this substance to be capable of transforming an unlimited quantity of oxalic acid.

Methanedicarboxylic or Malonic Acid, $COOH \cdot CH_2 \cdot COOH$.

164. The constitution of *malonic acid* is proved by its synthesis from monochloroacetic acid. Boiling an aqueous solution of potassium monochloroacetate with potassium cyanide forms cyanoacetic acid, convertible into malonic acid by hydrolysis of the cyano-group:

$$\underset{\text{Monochloroacetic acid}}{CH_2<\begin{matrix}Cl\\COOH\end{matrix}} \rightarrow \underset{\text{Cyanoacetic acid}}{CH_2<\begin{matrix}CN\\COOH\end{matrix}} \rightarrow \underset{\text{Malonic acid}}{CH_2<\begin{matrix}COOH\\COOH.\end{matrix}}$$

Malonic acid is a crystalline substance, and some of its physical properties are given in the table in **161**. When heated somewhat above its melting-point, it loses one molecule of carbon dioxide, being converted into acetic acid:

$$COOH \cdot CH_2 \cdot \boxed{COO}H = CO_2 + COOH \cdot CH_3.$$

The effect of heating above its melting-point a compound with two carboxyl-groups in union with one carbon atom is to eliminate one molecule of carbon dioxide from each molecule.

The most important derivative of malonic acid is *diethyl malonate*, many important syntheses being accomplished by its aid. It is a liquid of faint odour, boiling at 198°, and having at 15° the density 1·061. With sodium in the proportion of one atom to each molecule of ester, hydrogen is evolved, and the diethyl malonate is converted into a solid mass. In this reaction, hydrogen is replaced by sodium, yielding *diethyl monosodiomalonate*, a compound of the structure

$$\begin{matrix}COOC_2H_5\\ \dot{C}HNa\\ \dot{C}OOC_2H_5\end{matrix}$$

This constitution is indicated by the action of an alkyl halide (iodide), a sodium halide and an ester being obtained:

$$C_2H_5\boxed{I+Na}CH(COOC_2H_5)_2 = C_2H_5\cdot CH(COOC_2H_5)_2 + NaI.$$

On saponification, this ester yields a homologue of malonic acid.

If two atoms of sodium, instead of one, react with one molecule of diethyl malonate, two hydrogen atoms are replaced. Each of these hydrogen atoms is in the methylene-group, contact of the disodio-compound with two molecules of an alkyl iodide replacing the two sodium atoms by alkyl, with production of a substance converted by saponification into a homologue of malonic acid:

$$\begin{array}{l} COOC_2H_5 \\ \dot{C}\boxed{Na_2+2I}C_2H_5 \\ COOC_2H_5 \end{array} = 2NaI + \begin{array}{l} COOC_2H_5 \\ \dot{C}(C_2H_5)_2 \\ COOC_2H_5 \end{array}.$$

It is possible also to introduce two different alkyl-groups into diethyl malonate. Diethyl monosodiomalonate reacts with *methyl* iodide to form the diethyl ester of methylmalonic acid; with sodium this derivative yields another sodium compound, converted by *ethyl* iodide into the diethyl ester of methylethylmalonic acid. The reaction is discussed further in the chapter on tautomerism (**235**).

These examples indicate the possibility of synthesizing a great number of dibasic acids from diethyl malonate. The presence in each of these acids of two carboxyl-groups in union with the same carbon atom, and the resemblance of each to malonic acid displayed in the property of losing from each molecule a molecule of carbon dioxide through heating above the melting-point, makes evident the applicability of the so-called "malonic-ester synthesis" also to the preparation of the monobasic fatty acids. This process is exemplified by the action of heat on methylethylmalonic acid, each molecule losing a molecule of carbon dioxide with formation of methylethylacetic acid, identical in constitution with active valeric acid (**47**), and resoluble into two active components:

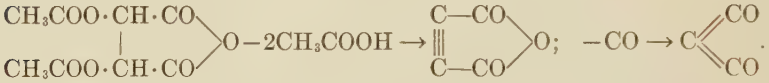
$$\begin{array}{l} COOH \\ CH_3\cdot\dot{C}\cdot C_2H_5 \\ \boxed{COO}H \end{array} = \begin{array}{l} COOH \\ CH_3\cdot\dot{C}\cdot C_2H_5. \\ H \end{array}$$

Methylethylmalonic acid — Valeric acid

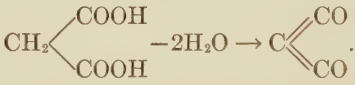
The malonic-ester synthesis is employed extensively in the preparation of acids, and will be the subject of frequent reference.

For the synthetic production of the higher dibasic acids of this series scheduled in the table of **161** various methods are available. An example is the reduction by sodium and boiling alcohol of the ester of *heptanedicarboxylic acid*-1:7 or azelaic acid to the corresponding diol, *nonanediol*-1:9 (**92**). Dry gaseous hydrogen bromide at 150° transforms this diol into *dibromononane*-1:9, convertible by the malonic-ester synthesis through elimination of two molecules of carbon dioxide into *undecanedicarboxylic acid*-1:11, a dibasic acid with four more carbon atoms than its parent substance. A dibasic acid with only two additional carbon atoms can be obtained by the interaction of *dibromononane*-1:9 and potassium cyanide, followed by hydrolysis of the dicarbonitrile formed.

165. *Carbon suboxide*, C_3O_2, is prepared best by bringing diacetyltartaric anhydride (**191**) in the gaseous state into contact with a red-hot platinum-wire, in accordance with the scheme



Its structure follows from its formation by the distillation of dry malonic acid with ten times its weight of phosphoric oxide:



Carbon suboxide is stable only at low temperatures; at the ordinary temperature it polymerizes in the course of a single day to a blackish-red amorphous mass.

It is a gas of very pungent odour, and can be condensed to a liquid boiling at 6° and solidifying at −111·3°. With water it regenerates malonic acid, indicating it to be an anhydride of that acid. The true anhydride,

analogous to the anhydrides of the higher homologues of malonic acid, does not exist.

Compounds containing the group $CH_2{=}CO$ are known, and are designated *ethenones* or *ketens*. Carbon suboxide is the simplest *diketen*.

Ethane-1:2-dicarboxylic or Succinic Acid, $COOH \cdot CH_2 \cdot CH_2 \cdot COOH$.

166. *Succinic acid* is a crystalline substance melting at 182°, and dissolving with difficulty in cold water. It is present in amber, in fos-

silized wood, and in many plants, and can be prepared synthetically by the following methods.

1. From ethene bromide by means of potassium cyanide, the dicyanoethane, $CN \cdot CH_2 \cdot CH_2 \cdot CN$, formed being hydrolyzed to succinic acid.

2. From malonic acid by the interaction of diethyl monosodiomalonate and ethyl monochloroacetate:

$$(COOC_2H_5)_2CH\boxed{Na+Cl}H_2C \cdot COOC_2H_5 =$$
$$= NaCl + (COOC_2H_5)_2CH \cdot CH_2 \cdot COOC_2H_5.$$

In this reaction an ester of *ethanetricarboxylic acid* is formed. At temperatures above its melting-point, each molecule of the corresponding acid loses one molecule of carbon dioxide, yielding succinic acid:

$$\boxed{COO}H \cdot \dot{C}H \cdot COOH \rightarrow \begin{matrix} CH_2 \cdot COOH \\ \dot{C}H_2 \cdot COOH. \end{matrix}$$

Succinic acid and symmetrically substituted succinic acids can be obtained also by the action of an ethereal solution of iodine or bromine on diethyl monosodiomalonate or its monoalkyl-derivatives:

$$\begin{matrix} COOC_2H_5 \\ A \cdot \dot{C}\boxed{Na} \\ \dot{C}OOC_2H_5 \end{matrix} \quad \begin{matrix} \\ +I_2+\boxed{Na}\dot{C} \cdot A' \\ \end{matrix} \quad \begin{matrix} COOC_2H_5 \\ \dot{C}OOC_2H_5 \end{matrix} = \begin{matrix} COOC_2H_5 & COOC_2H_5 \\ A \cdot \dot{C}\text{———}\dot{C} \cdot A' \\ \dot{C}OOC_2H_5 & \dot{C}OOC_2H_5 \end{matrix} + 2NaI.$$

A = Hydrogen or alkyl — Tetracarboxylic ester

By saponification and elimination of carbon dioxide the ester formed is converted into the dibasic acid:

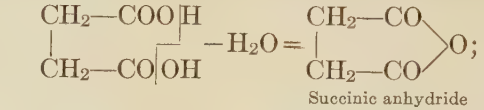
$$\begin{matrix} COOH & COOH \\ A \cdot \dot{C}\text{———}\dot{C} \cdot A' \\ \boxed{COO}H & \boxed{COO}H \end{matrix} = \begin{matrix} A \cdot CH \cdot COOH \\ A' \cdot \dot{C}H \cdot COOH \end{matrix} + 2CO_2.$$

Unlike calcium oxalate, *calcium succinate* is soluble in water. A characteristic salt is *ferric succinate*, deposited as an amorphous, flocculent, brownish-red precipitate by mixing solutions of ferric chloride and an alkali-metal succinate.

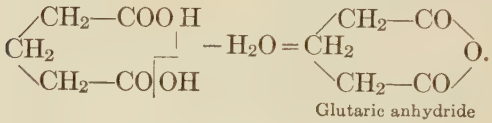
Formation of Anhydrides.

167. Oxalic acid and malonic acid do not yield anhydrides (165), but succinic acid, $C_4H_6O_4$, and glutaric acid, $C_5H_8O_4$, give them very readily. The formation of anhydride is due to the elimination of one

molecule of water from one molecule of the dibasic acid, as is proved by a determination of the molecular weights of the anhydrides:



Succinic anhydride



Glutaric anhydride

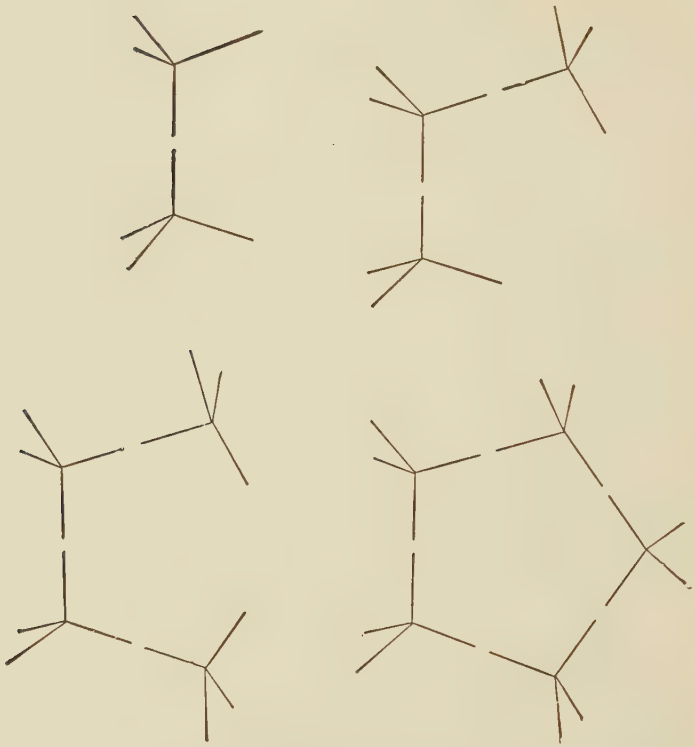


Fig. 31.—Spacial Representation of the Bonds between 2 to 5 Carbon Atoms.

These anhydrides are reconverted into the corresponding dibasic acids by dissolving them in water.

A derivative of succinic acid, *succinimide*, $\begin{matrix}CH_2\cdot CO\\ |\\ CH_2\cdot CO\end{matrix}\!\!>\!NH$, has a ring of four carbon atoms and one nitrogen atom, and is formed by the rapid

distillation of ammonium succinate. The atoms situated at the extremities of a carbon chain of four or five carbon atoms interact very readily; but those in shorter chains interact only with difficulty, or not at all. Analogous phenomena are the elimination of one molecule of water from $\alpha\alpha'$-glycols (150), and of ammonia from $\alpha\alpha'$-diamines (159), both effected very readily with a carbon chain of four or five carbon atoms, but with a shorter chain either impossible or leading to the formation of very unstable compounds. A satisfactory explanation of these phenomena and of others of similar type, can be attained by a consideration of the direction of the bonds in space. In 48 the four affinities of the carbon atom were assumed to be directed towards the angles of a regular tetrahedron with the carbon atom at the centre. For a single bond between two carbon atoms one affinity of each of these atoms is supposed to be attached to one affinity of the other (Fig. 31). The position in space of the carbon atoms in a chain of three or more members, and the direction of their affinities, are represented in the figure.

Obviously in a normal chain of four carbon atoms the affinities at the extremities approach one another closely, and in a chain of five carbon atoms still more closely, thus facilitating ready interaction.

A few instances are known of compounds with a closed chain containing only two carbon atoms, such as epoxyethane, $\begin{matrix} CH_2 \cdot CH_2 \\ \diagdown\!\diagup \\ O \end{matrix}$. The figure indicates for two carbon atoms the necessity for a considerable change in the directions of the affinities to render the formation of a ring possible. Such compounds are unstable, the closed chain being opened very readily, as is indicated by the "strain-theory" of VON BAEYER (120).

The Saponification of Esters of Polyhydric Alcohols and of Polybasic Acids.

168. Esters can be saponified by means of either acids or alkalis. In the saponification with acid of the esters of symmetrical dibasic acids and of the esters of dihydric alcohols, the process does not take place step-by-step, and the remarkable fact of the ratio of the saponification-constants of the neutral and the acid esters, or of the neutral and the alcoholic esters, being as 2 : 1 has been established. This phenomenon is exemplified by the saponification with acid of glycol diacetate, a process unattended by the intermediate formation of monoacetate, the velocity-constant being twice as great as that for glycol monoacetate. A similar ratio exists between the constants for diethyl malonate and ethyl hydrogen malonate.

There is a simple theoretical explanation of this phenomenon. In the acid saponification the hydrogen ions exert a catalytic action, and the saponification may be assumed to be due to the impacts of the ions with the ester molecules. The hydrogen ions being much smaller than these molecules, localization of the impacts to ester-groups can be considered the cause of saponification. For equimolecular concentration the impacts are twice as numerous for the esters of dihydric alcohols or of dibasic acids as for mono-esters, as can be tested by a doubling of the concentration of the ester of a monohydric alcohol and of a monobasic acid.

For esters like those of methylsuccinic acid,

$$COOH \cdot CH(CH_3) \cdot CH_2 \cdot COOH,$$

the lack of structural symmetry prevents the molecule consisting of two similar parts, and the velocity-constants are not in the ratio 2 : 1. On saponification, such esters should behave as a mixture of two dissimilar esters, and experiment has confirmed this view.

In the saponification with alkali of the esters of polyhydric alcohols, the saponification-constants exhibit a similar ratio. If the constant for glyceryl monoacetate be 1, that for the diacetate is 2, and that for the triacetate 3. In this instance the hydroxyl-ions exert a catalytic action, and the explanation of the simple ratio of the constants is similar to that given for the hydrogen ions. Obviously the existence of these ratios is contingent on instantaneous saponification of the esters, and it would be incompatible with the step-by-step process formerly assumed to occur.

For the saponification by alkalis of the esters of polybasic acids the ratio of the constants is entirely different, the numerical value of the constant for the normal ester being many times greater than that for the primary ester. This phenomenon is exemplified by the saponification-velocities of diethyl malonate and ethyl hydrogen malonate, their ratio being almost 100 : 1. This fact is explicable on the assumption of step-by-step saponification, the process inducing the presence in the alkaline solution of the primary ester of many anions such as

$$C_2H_5OOC \cdot CH_2 \cdot COO',$$

the primary ester existing in this solution as a highly-ionized salt. The saponifying action of the negatively-charged hydroxyl-ions is inhibited in great measure by the repellent influence of the similarly-charged anions.

II. UNSATURATED DIBASIC ACIDS.

Fumaric Acid and Maleic Acid, $C_4H_4O_4$.

169. The most important members of the group of unsaturated dibasic acids are *fumaric acid* and *maleic acid*, both with the formula $C_4H_4O_4$. They have been investigated exhaustively, a complete explanation of their isomerism having been attained finally by an application of the principles of stereoisomerism.

Fumaric acid is distributed somewhat widely in the vegetable kingdom. It does not melt at the ordinary pressure, but sublimes in the neighbourhood of 200°; and it dissolves with difficulty in water. Maleic acid is not a natural product; it melts at 130°, and is very readily soluble in water.

Each acid can be obtained by heating malic acid (**187**),

$$COOH \cdot CHOH \cdot CH_2 \cdot COOH,$$

the effect depending on the temperature and duration of the reaction. Fumaric acid is the principal product of prolonged heating between 140° and 150°, but exposure to a higher temperature yields a distillate consisting of the anhydride of maleic acid and water. This anhydride takes up water readily, regenerating the acid. These processes constitute the ordinary methods for the preparation of these acids, and they indicate both to have the same structural formula:

$$\underset{\boxed{OH\ H}}{COOH \cdot \dot{C}H \cdot \dot{C}H \cdot COOH} - H_2O = COOH \cdot CH{:}CH \cdot COOH.$$

This view of their constitution is supported by the conversion of each acid into succinic acid by means of sodium-amalgam and water, and also by the formation of monobromosuccinic acid by addition of hydrogen bromide, and of malic acid by heating with water at a high temperature. Both acids therefore have the same constitutional formula,

$$COOH \cdot CH{:}CH \cdot COOH.$$

The isomerism of the crotonic acids is similar (**136**). It remains to consider how this isomerism can be explained by the aid of stereochemistry.

170. A single bond between two carbon atoms may be represented (**167**) as in Fig. 32. If the tetrahedra be drawn in full, the single bond

will be as in Fig. 33. If the tetrahedra be free to rotate round their common axis, isomerism cannot be expected for compounds *Cabc*—*Cdef*, nor has it been observed.

With a double bond, two affinities of each carbon atom come into

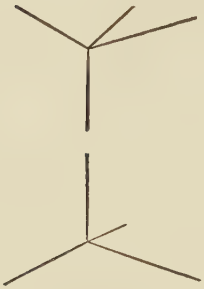


Fig. 32.

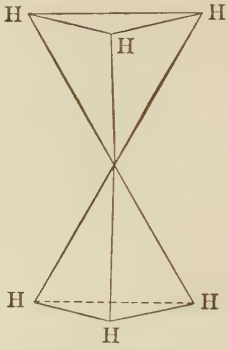
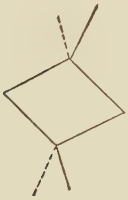


Fig. 33.

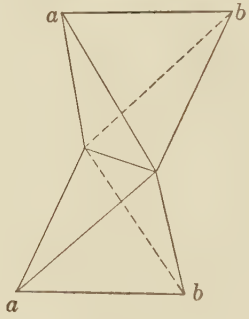
Single Bond between two Carbon Atoms.

play, as represented graphically in Figs. 34, 35, and 36, free rotation of the tetrahedra relative to one another being no longer possible.

The figures indicate difference of grouping to depend on the position of the groups *a* and *b* of one tetrahedron with reference to the similar



or



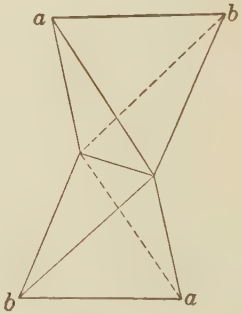


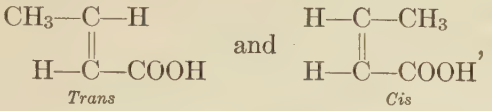
Fig. 34. Fig. 35. Fig. 36.

Graphic Spacial Representation of the Double Bond between two Carbon Atoms.

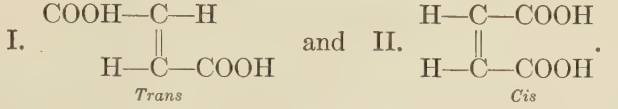
groups *a* and *b* of the other. Group *a* may be over *a*, and *b* over *b*, as in Fig. 35; or *a* may be over *b*, and *b* over *a*, as in Fig. 36. These positions can be represented by the formulæ

$$\begin{matrix} a\text{—}C\text{—}b \\ \| \\ a\text{—}C\text{—}b \end{matrix} \quad \text{and} \quad \begin{matrix} a\text{—}C\text{—}b \\ \| \\ b\text{—}C\text{—}a \end{matrix},$$

the two crotonic acids being

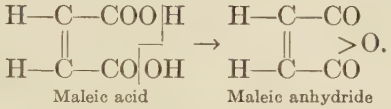


and fumaric and maleic acids having the formulæ



It is necessary now to identify the formula of fumaric acid and that of maleic acid.

Maleic acid yields an anhydride, while fumaric acid does not. In formula II the carboxyl-groups are in juxtaposition, but in formula I they are removed from each other so far as possible. Only in the acid with the *cis*-formula are the carboxyl-groups represented in a position to interact readily:



Hence *fumaric acid is inferred to have the constitution indicated in formula* I, *and maleic acid that corresponding with formula* II. Another example in support of this explanation is mentioned in **194.**

171. Maleic acid can be converted into fumaric acid by keeping it for some time at a temperature above its melting-point; by bringing it into contact with hydrogen halides at the ordinary temperature; by exposing its concentrated solution in presence of a trace of bromine to the action of sunlight, a slow reaction in absence of light; by contact of ethyl maleate with a small proportion of iodine; or by other means. The facility of all these decompositions indicates maleic acid to be the unstable form, and fumaric acid the stable modification. Inversely, fumaric acid is converted by distillation into maleic anhydride. Fumaric acid is transformed also into maleic acid by the action of ultraviolet light, as is maleic acid into fumaric acid. With increasing concentration of the initial solution, the equilibrium attained is displaced towards the side of the maleic acid.

Affinity-constants of the Unsaturated Acids.

172. Like the monobasic unsaturated acids (135), the dibasic unsaturated acids have greater affinity-constants than the corresponding

saturated acids. For succinic acid, $10^4k = 0{\cdot}665$, and for fumaric acid, $10^4k = 9{\cdot}3$. The strength of acetylenedicarboxylic acid,

$$COOH{\cdot}C{\equiv}C{\cdot}COOH,$$

obtained by the interaction of alcoholic potash and dibromosuccinic acid,

$$COOH{\cdot}CHBr{—}CHBr{\cdot}COOH,$$

is equal approximately to that of sulphuric acid, the presence of a double bond, and even more of a triple bond, intensifying the acidic character. For maleic acid $10^4k = 117$, or about twelve times as much as for fumaric acid. This discrepancy indicates the great influence exerted on the strength of these acids by the distance between the carboxyl-groups in the molecule.

The ionization of dibasic acids is a step-by-step process. An acid H_2A yields first $H^{\cdot}+HA'$, and on further dilution HA' is ionized to $H^{\cdot}+A''$. In this dissociation remarkable differences have been observed. For some acids the second stage of ionization does not begin until the first is almost complete, but for other acids its inception corresponds approximately with the end of the initial half of the first stage. The degree of ionization depends on the relative position of the carboxyl-groups in the molecule. The nearer these groups are to each other, the more extended is the first stage and the smaller the second stage of ionization, and *vice-versa*.

This phenomenon is explained readily by assuming the negative charge of the anion to be concentrated on the hydroxyl-oxygen of the ionized carboxyl-group. During the ionization of the first hydrogen atom, the presence of one carboxyl-group promotes the ionization of the other. This influence is greatest with close proximity of the carboxyl-groups. Other negative groups produce a similar effect (**178** and **183**). After completion of the ionization of the first hydrogen atom, the HA′-residue is decomposed with difficulty into $H^{\cdot}$ and A'' on account of the attraction exerted by the negative charge of this residue on any positively-charged hydrogen ion liberated, this attraction being greatest when the negative charge is close to the hydrogen atom of the HA′-residue. On the assumption of this charge being situated on the hydroxyl-oxygen of the first carboxyl-group, its attraction is greatest for close proximity of the two carboxyl-groups in the non-ionized acid. If the hydrogen atom of the first carboxyl-group and the negatively-charged hydroxyl-oxygen of the HA′-residue be further apart, the second stage of the ionization meets with less resistance and therefore is facilitated.

Dibasic Acids with more than one Triple Bond.

173. VON BAEYER has prepared from acetylenedicarboxylic acid dibasic acids containing more than one triple bond in the molecule. Heat-

ing with water converts its potassium hydrogen salt into potassium propiolate (**139**), with elimination of carbon dioxide:

$$KOOC\cdot C{\equiv}C\cdot\boxed{CO_2}H = CO_2 + KOOC\cdot C{\equiv}CH.$$

The copper derivative of this salt, KOOC·C≡Ccu,* reacts with potassium ferricyanide in alkaline solution to form cupric oxide, the two acid-residues uniting simultaneously with production of the potassium salt of *diacetylene-dicarboxylic acid*,

$$KOOC\cdot C{\equiv}C{-}C{\equiv}C\cdot COOK.$$

The potassium hydrogen salt of this acid also loses carbon dioxide readily, and the copper derivative of the monobasic acid formed is converted by similar oxidation into cupric oxide and the potassium salt of *tetra-acetylene-dicarboxylic acid*:

$$2KOOC\cdot C{\equiv}C\cdot C{\equiv}Ccu\ ^* \rightarrow KOOC\cdot C{\equiv}C\cdot C{\equiv}C\cdot C{\equiv}C\cdot C{\equiv}C\cdot COOK.$$

These compounds are very unstable, being decomposed by the action of light and otherwise.

III. HIGHER POLYBASIC ACIDS.

174. Except as esters, acids with three carboxyl-groups in union with one carbon atom are unknown. The triethyl ester of *methanetricarboxylic acid* is obtained by the action of ethyl chlorocarbonate (**263**) on diethyl monosodiomalonate:

$$C_2H_5OOC\boxed{Cl+Na}CH(COOC_2H_5)_2 \rightarrow C_2H_5OOC\cdot CH(COOC_2H_5)_2.$$

Ethyl chlorocarbonate

Saponification of this ester is attended by elimination of carbon dioxide, malonic acid being formed instead of the corresponding tribasic acid. This phenomenon affords another instance of the tendency for several *negative groups not to remain in union with one carbon atom*, two being the maximum number for carboxyl (**149** and **177**).

A description of the syntheses of a few of the polybasic acids will exemplify the methods adopted for the preparation of compounds of this class.

A type of the *tribasic acids* is *propane*-1:2:3-*tricarboxylic acid*, or tricarballylic acid, obtainable by several methods.

1. From 1:2:3-tribromopropane by means of potassium cyanide, and hydrolysis of the tricyanopropane formed:

$$\begin{array}{llll} CH_2{-}CH{-}CH_2 & CH_2{-}CH{-}CH_2 & CH_2{-}{-}CH{-}{-}CH_2 \\ \dot{B}r\quad \dot{B}r\quad \dot{B}r & \rightarrow \dot{C}N\quad \dot{C}N\quad \dot{C}N & \rightarrow \dot{C}OOH\quad \dot{C}OOH\quad \dot{C}OOH \end{array}$$

* cu = ½Cu.

2. From diethyl disodiomalonate and ethyl monochloroacetate:

$$(C_2H_5OOC)_2C\boxed{Na_2+2Cl}CH_2\cdot COOC_2H_5=$$

$$=\begin{matrix}C_2H_5OOC\\C_2H_5OOC\end{matrix}>C<\begin{matrix}CH_2\cdot COOC_2H_5\\CH_2\cdot COOC_2H_5\end{matrix}+2NaCl.$$

Saponification of this ester yields an acid convertible by heat into tricarballylic acid, carbon dioxide being eliminated:

$$\begin{matrix}HOOC\\H\boxed{O_2C}\end{matrix}>\dot{C}\begin{matrix}CH_2\cdot COOH\\CH_2\cdot COOH\end{matrix}\rightarrow\dot{C}H\cdot COOH\,.\begin{matrix}CH_2\cdot COOH\\CH_2\cdot COOH\end{matrix}$$

A synthesis peculiar to the polybasic acids consists in the *addition* of ethyl monosodiomalonate to the esters of unsaturated acids such as fumaric acid:

$$\begin{matrix}Na\\|\\HC(COOC_2H_5)_2\end{matrix}+\begin{matrix}CH\cdot COOC_2H_5\\\|\\CH\cdot COOC_2H_5\end{matrix}=\begin{matrix}NaCH\cdot COOC_2H_5\\|\\CH\cdot COOC_2H_5\\|\\CH(COOC_2H_5)_2\end{matrix}\,.$$

Saponification and subsequent elimination of carbon dioxide yield tricarballylic acid. It melts at 166°, and dissolves readily in water.

Propene-1:2:3-*tricarboxylic* or *aconitic acid* melts at 191°, and is a type of the *unsaturated tribasic acids.* It is obtained from citric acid (**197**) through removal of water by heating. The constitution of aconitic acid is

$$\begin{matrix}CH\!=\!=\!=C\!-\!-\!-\!-CH_2\\\dot{C}OOH\ \dot{C}OOH\ \ \dot{C}OOH\end{matrix}$$

for reduction converts it into propane-1:2:3-tricarboxylic acid.

SUBSTITUTED ACIDS.

I. HALOGEN-SUBSTITUTED ACIDS.

175. The *halogen-substituted acids* can be obtained by the direct action of chlorine or bromine on the saturated fatty acids, but this process is not very satisfactory. The best method of preparing the monochloro-acids and monobromo-acids is the action of chlorine or bromine on the acid chloride or bromide.

In this reaction it is sufficient to add a small proportion of the acid halide to the acid, the method for the technical production of monochloroacetic acid. The normal course of the reaction is indicated by schemes I and II:

$$\text{I. } R\cdot CH_2\cdot COBr + Br_2 \rightarrow R\cdot CHBr\cdot COBr + HBr.$$

The brominated acid bromide then reacts with the acid:

$$\text{II. } R\cdot CHBr\cdot COBr + R\cdot CH_2\cdot COOH \rightarrow R\cdot CHBr\cdot COOH + R\cdot CH_2\cdot COBr.$$

In the second stage the unbrominated acid bromide is regenerated, and becomes available for further bromination.

The formation in this reaction of 1-substituted acids only is explicable on the assumption of a primary transformation of the acid bromide into an isomeride:

$$R\cdot CH_2\cdot COBr \rightarrow R\cdot CH{:}C{<}\begin{matrix}OH\\Br\end{matrix}.$$

Addition of bromine to this compound yields a substance of the formula

$$R\cdot CHBr\cdot C{<}\begin{matrix}OH\\Br\\Br\end{matrix},$$

convertible by the elimination of one molecule of hydrogen bromide into an acid bromide brominated at carbon atom 1.

Halogen-substituted acids can be prepared also by addition of hydrogen halide or halogen to the unsaturated acids, or by the action of phosphorus halides on the hydroxy-acids. Sometimes the iodo-acids can be obtained advantageously from the corresponding chloro-derivatives by heating them with potassium iodide.

176. The introduction of halogen into the molecule causes a marked increase in the strength of an acid, as will be seen from the table below of dissociation-constants, 10^4k. This table indicates the strength of an acid to be increased to a greater extent by chlorine than by bromine,

and by bromine than by iodine, and a marked increase to be occasioned by the introduction of more than one chlorine atom. The position of the halogen atom also exerts an influence, the value of the constant for iodoacetic acid with the iodine atom in the 1-position being thirty-two times as great as for acetic acid, but for 2-iodopropionic acid only seven times as great as for propionic acid.

Name.	Formula.	10^4k.
Acetic acid	$CH_3 \cdot CO_2H$	0·18
Monochloroacetic acid	$CH_2Cl \cdot CO_2H$	15·5
Monobromoacetic acid	$CH_2Br \cdot CO_2H$	13.8
Monoiodoacetic acid	$CH_2I \cdot CO_2H$	7·5
Dichloroacetic acid	$CHCl_2 \cdot CO_2H$	514
Trichloroacetic acid	$CCl_3 \cdot CO_2H$	12100
Butyric acid	$CH_3 \cdot CH_2 \cdot CH_2 \cdot CO_2H$	0·152
1-Chlorobutyric acid	$CH_3 \cdot CH_2 \cdot CHCl \cdot CO_2H$	13·9
2-Chlorobutyric acid	$CH_3 \cdot CHCl \cdot CH_2 \cdot CO_2H$	0·89
3-Chlorobutyric acid	$CH_2Cl \cdot CH_2 \cdot CH_2 \cdot CO_2H$	0·3 (*ca.*)

The influence of the carboxyl-groups on the halogen atoms is such as to cause *the properties of the monohalogen-substituted acids to depend chiefly on the relative positions of the halogen atom and the carboxyl-group.*

On boiling with alkalis, the 1-halogen-substituted acids are converted readily into the 1-hydroxy-acids by exchange of halogen for hydroxyl:

$$\underset{\text{Monochloroacetic acid}}{CH_2Cl \cdot COOH} + 2KOH = KCl + \underset{\text{Potassium glycollate}}{CH_2OH \cdot COOK} + H_2O.$$

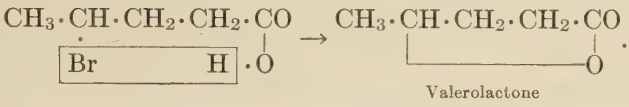
A similar process eliminates hydrogen halide from the 2-halogen-substituted acids, with formation of unsaturated acids:

$$\underset{\text{2-Chlorobutyric acid}}{CH_3 \cdot CHCl \cdot CH_2 \cdot COOH} = \underset{\text{Crotonic acid}}{CH_3 \cdot CH{:}CH \cdot COOH} + HCl.$$

The behaviour of the 2-halogen-substituted acids with sodium carbonate is very characteristic. Warming with its aqueous solution removes hydrogen halide and carbon dioxide simultaneously from the molecule, with formation of an unsaturated hydrocarbon:

$$CH_3 \cdot \underset{\boxed{Br}}{CH} \cdot \overset{\diagup CH_3}{CH} \mid CO_2 \boxed{Na} = \underset{\text{2-Butene}}{CH_3 \cdot CH{:}CH \cdot CH_3} + NaBr + CO_2.$$

On boiling with water or with an alkali-metal carbonate, the 3-halogen-substituted acids lose hydrogen halide readily, forming *lactones* (180, 185, 186):



Valerolactone

Chloroacetic Acids.

177. *Monochloroacetic acid*, $CH_2Cl \cdot COOH$, is obtained by the action of chlorine on acetic acid in presence of a small proportion of acetic anhydride or acetyl chloride as catalyst (**175**). A mode of preparation also employed technically involves the action of water on trichloroethene with sulphuric acid as catalyst:

$$CHCl{:}CCl_2 + 2H_2O = CH_2Cl \cdot COOH + 2HCl.$$

It is a crystalline solid melting at 63° and boiling at 186°. *Dichloroacetic acid*, $CHCl_2 \cdot COOH$, a liquid boiling at 191°, and also *trichloroacetic acid*, $CCl_3 \cdot COOH$, a solid melting at 57° and boiling at 195°, are prepared conveniently from chloral (**201**). Trichloroacetic acid is unstable, boiling with water decomposing it into carbon dioxide and chloroform:

$$CCl_3 \cdot \boxed{CO_2}H = CCl_3H + CO_2.$$

This reaction is another example of the molecular instability induced by "loading" a carbon atom with negative elements and groups.

A synthesis of acetic acid of historical importance was effected by Kolbe in the year 1845. Trichloroacetic acid is an intermediate product, and is converted into acetic acid by reduction with sodium-amalgam and water. The initial stage in the synthesis of trichloroacetic acid is the union at high temperature of carbon and sulphur to carbon disulphide, CS_2. This substance is transformed by chlorine into tetrachloromethane, CCl_4, convertible into tetrachloroethene, C_2Cl_4, by passing its vapour through a red-hot tube. In contact with water tetrachloroethene reacts with chlorine under the influence of sunlight to form trichloroacetic acid:

$$CCl_2{:}CCl_2 + Cl_2 \rightarrow CCl_3 \cdot CCl_3;\ +3H_2O \rightarrow CCl_3 \cdot C(OH)_3;\ -H_2O \rightarrow CCl_3 \cdot COOH.$$

Acids with more than one Halogen Atom in the Molecule.

178. Isomerism in this type of compounds can be occasioned by a difference in position of the halogen atoms in the molecule. Addition of halogen to an unsaturated acid produces a compound with the halogen atoms attached to adjoining carbon atoms.

The elimination of hydrogen halide from acids of this class affords a striking example of the value of stereochemistry in explaining phenomena inexplicable by the ordinary constitutional formulæ. Among them is the fact that in the series of unsaturated acids each molecule of the dibromide of one modification loses two molecules of hydrogen bromide very readily, yielding an acid with a triple bond, while the dibromide of the other modi-

fication either does not react thus, or only with difficulty. An example of this difference is afforded by erucic and brassidic acids, substances proved by the method indicated in **140** to have the constitution

$$C_8H_{17}\cdot CH{:}CH\cdot C_{11}H_{22}\cdot COOH.$$

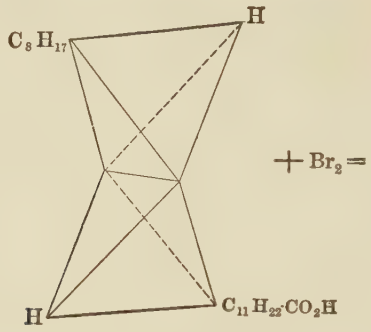


Fig. 37.—Erucic Acid.
Trans-formula.

When heated with alcoholic potash between 150° and 170°, dibromoerucic acid, obtained by addition of bromine to erucic acid, loses readily from each molecule two molecules of hydrogen bromide, yielding *behenolic acid*, $C_8H_{17}\cdot C{\equiv}C\cdot C_{11}H_{22}\cdot COOH$; whereas one molecule of hydrogen bromide

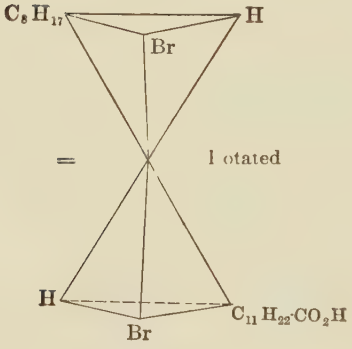


Fig. 38.—Dibromoerucic Acid.

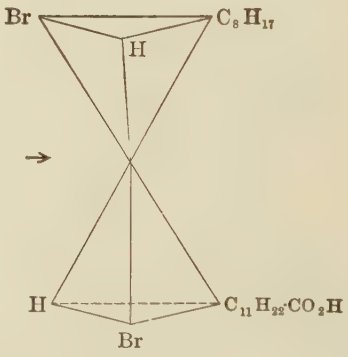


Fig. 39.—Dibromoerucic Acid.
Each hydrogen atom in corresponding position with a bromine atom.

is eliminated from each molecule of dibromobrassidic acid, with production of a monobromoerucic acid. This difference is expressed by assigning the *trans*-formula to erucic acid and the *cis*-formula to brassidic acid, as indicated in Fig. 37 to 42.

In the formula for dibromoerucic acid, the tetrahedra can be rotated to bring each bromine atom above a hydrogen atom, making possible the

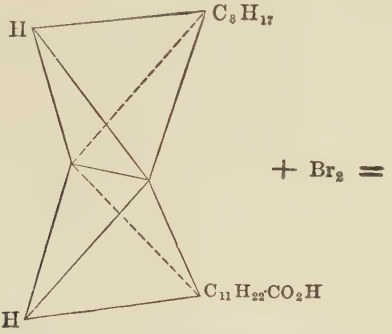


Fig. 40.—Brassidic Acid.
Cis-formula.

elimination of two molecules of hydrogen bromide (Figs. 38 and 39); in that for dibromobrassidic acid, only one bromine atom and one hydrogen atom can be brought into the "corresponding positions" (Figs. 41 and 42).

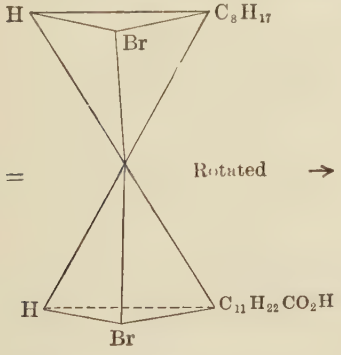


Fig. 41.—Dibromobrassidic Acid.

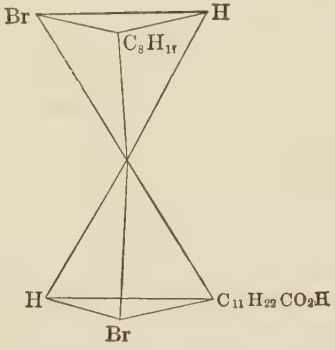


Fig. 42.—Dibromobrassidic Acid.
Only one hydrogen atom in corresponding position with a bromine atom.

II. MONOBASIC HYDROXY-ACIDS.

179. The *hydroxy-acids* are substances with one or more hydroxyl-groups and carboxyl-groups in the molecule. The general methods for their formation depend on the introduction of hydroxyl-groups and carboxyl-groups. They are produced in the following reactions.

1. By the careful oxidation of polyhydric alcohols:

$$\underset{\text{Propane-1:2-diol}}{CH_3\cdot CHOH\cdot CH_2OH} \rightarrow \underset{\text{Lactic acid}}{CH_3\cdot CHOH\cdot COOH}.$$

2. By replacement of the halogen in halogen-substituted acids by hydroxyl, as described in **150**.

3. By reduction of the aldehydic acids and ketonic acids, each type having both a carboxyl-group and a carbonyl-group:

$$\underset{\text{Pyruvic acid}}{CH_3\cdot CO\cdot COOH} + 2H = \underset{\text{Lactic acid}}{CH_3\cdot CHOH\cdot COOH}.$$

4. By the action of nitrous acid on acids with an amino-group in the alkyl-residue:

$$\underset{\text{Glycine}}{NH_2\cdot CH_2\cdot COOH} + HNO_2 = \underset{\text{Glycollic acid}}{CH_2OH\cdot COOH} + N_2 + H_2O.$$

5. By addition of hydrogen cyanide to aldehydes or ketones, and hydrolysis of the carbonitrile obtained (**101**, 3), a method yielding only 1-hydroxy-acids:

$$\underset{\text{Aldehyde}}{C_nH_{2n+1}\cdot CHO} + HCN = \underset{\text{Cyanohydrin}}{C_nH_{2n+1}\cdot C\begin{matrix}H\\CN\\OH\end{matrix}};$$

$$\underset{\text{Cyanohydrin}}{C_nH_{2n+1}\cdot C\begin{matrix}H\\CN\\OH\end{matrix}} + 2H_2O = \underset{\text{1-Hydroxy-acid}}{C_nH_{2n+1}\cdot C\begin{matrix}H\\COOH\\OH\end{matrix}} + NH_3.$$

By exchange of bromine for hydroxyl, acids brominated by the method described in **175** yield hydroxy-acids identical with those obtained by this *cyanohydrin-synthesis*, proving the bromine in these acids to be in union with the 1-carbon atom.

6. Oxidation with potassium permanganate effects the direct replacement of hydrogen by hydroxyl in acids with a hydrogen atom linked to a tertiary carbon atom:

$$\underset{\text{\textit{iso}Butyric acid}}{\begin{matrix}CH_3\\CH_3\end{matrix}>CH\cdot COOH} + O = \underset{\text{1-Hydroxy\textit{iso}butyric acid}}{\begin{matrix}CH_3\\CH_3\end{matrix}>C(OH)\cdot COOH}.$$

Properties.

180. Substitution in the hydroxyl-group of the hydroxy-acids yields compounds different from those obtained by substitution in the carboxyl-group. Replacement of the hydrogen atom of the hydroxyl-group by alkyl produces a *primary ether*:

$$\underset{\text{Glycollic acid}}{CH_2OH\cdot COOH} \rightarrow \underset{\text{Ethylglycollic acid}}{CH_2OC_2H_5\cdot COOH}.$$

Like an ordinary ether, $C_nH_{2n+1}\cdot O\cdot C_mH_{2m+1}$, ethylglycollic acid cannot be saponified. The corresponding exchange of the hydrogen atom of the carboxyl-group for alkyl produces an ester:

$$CH_2OH\cdot COOH \rightarrow CH_2OH\cdot COOC_2H_5.$$
Ethyl glycollate

Like other esters, these compounds can be saponified.

The introduction of hydroxyl strengthens the fatty acids to an extent dependent on its position relative to the carboxyl-group, an effect analogous to that produced by the halogens (176). This characteristic is indicated by the table of the values for several acids of the dissociation-constant 10^4k.

Name.	Formula.	10^4k.
Acetic acid	$CH_3\cdot COOH$	0·180
Glycollic acid (Hydroxyacetic acid)	$CH_2OH\cdot COOH$	1·52
Propionic acid	$CH_3\cdot CH_2\cdot COOH$	0·134
Lactic acid (1-Hydroxypropionic acid)	$CH_3\cdot CHOH\cdot COOH$	1·38
2-Hydroxypropionic acid	$CH_2OH\cdot CH_2\cdot COOH$	0·311

Heating eliminates water readily from the 1-*hydroxy-acids*, and removes two molecules simultaneously from two molecules of acid, the reaction being between the hydroxyl-group of one molecule and the carboxyl-group of the other. Lactic acid yields *lactide*:

$$\begin{array}{l} CH_3\cdot CH(OH\ H)\ OOC \\ \qquad\qquad | \qquad\quad | \\ \quad COO(H\ HO)\text{—}CH\cdot CH_3 \end{array} = 2H_2O + \begin{array}{l} CH_3\cdot CH\cdot OOC \\ \qquad\quad | \qquad\quad | \\ \quad COO\text{—}CH\cdot CH_3. \end{array}$$
Lactide

This formula of this compound indicates it to be a double ester, its constitution being proved by its behaviour with boiling water or dilute acids; like the esters, it is saponified, yielding lactic acid.

2-*Hydroxy-acids* give up water readily, with formation of unsaturated acids:

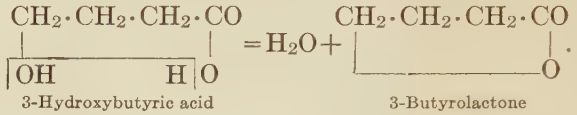
$$\begin{array}{l} CH_3\cdot CH\cdot CH\cdot COOH \\ \qquad\quad | \quad | \\ \quad (OH\ H) \end{array} = H_2O + CH_3\cdot CH{:}CH\cdot COOH$$
2-Hydroxybutyric acid — Crotonic acid

When a 2-hydroxy-acid is boiled with excess of ten per cent. solution of sodium hydroxide, it is converted partly into a Δ^1-unsaturated acid, and partly into a Δ^2-unsaturated acid. A portion remains unchanged, and an equilibrium is attained:

$$R\cdot CH{:}CH\cdot CH_2\cdot COOH \rightleftarrows R\cdot CH_2\cdot CHOH\cdot CH_2\cdot COOH \rightleftarrows$$
$$\rightleftarrows R\cdot CH_2\cdot CH{:}CH\cdot COOH.$$

For a reversible reaction the same equilibrium should be reached by starting from the hydroxy-acid, or from either of the two unsaturated acids, and FITTIG proved this transformation to conform with the rule.

3-*Hydroxy-acids* and 4-*hydroxy-acids* lose water, with formation of inner anhydrides termed *lactones* (176, 185, 186):

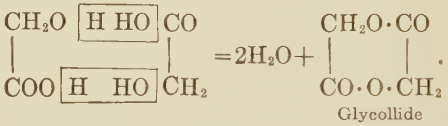


3-Hydroxybutyric acid — 3-Butyrolactone

Glycollic Acid, $C_2H_4O_3$.

181. *Glycollic acid* is present in unripe grapes. Usually it is prepared by the interaction of monochloroacetic acid and potassium hydroxide:

Glycollic acid is a crystalline solid melting at 80°. It is soluble in water, alcohol, and ether very readily; and the calcium salt dissolves in water with difficulty. Distillation of glycollic acid *in vacuo* eliminates water, and forms *glycollide:*



Glycollide

Hydroxypropionic Acids, $C_3H_6O_3$.

182. Two *hydroxypropionic acids* differing in the position occupied by the hydroxyl-group are known, 1-*hydroxypropionic acid,*

$$CH_3 \cdot CHOH \cdot COOH,$$

and 2-*hydroxypropionic acid,* $CH_2OH \cdot CH_2 \cdot COOH$. The first is ordinary *lactic acid.*

1-Hydroxypropionic acid can be obtained synthetically by the methods described in 179, although usually it is prepared by other means. In presence of the organized ferment termed the " Lactic-acid bacillus," sugars such as lactose, sucrose, and dextrose undergo " Lactic fermentation," ninety-five per cent. of the product being lactic acid. These bacilli are present in material such as decaying cheese, and cannot live in a solution of lactic acid of more than a certain concentration, fermentation being made possible by addition of chalk to neutralize the lactic acid formed. Lactic acid can be prepared also by heating dextrose or invert-sugar with sodium hydroxide.

Lactic acid derives its name from its presence in sour milk, as a result of the fermentation of the lactose present. The faint acidic odour possessed by sour milk is not due to lactic acid, but to traces of volatile fatty acids simultaneously formed, lactic acid being odourless. Lactic acid is present also in other fermented substances, such as pickled cabbage; and in large proportion in ensilage, a cattle-food prepared by submitting piles of grass or clover to pressure.

Lactic acid is purified by distilling the aqueous acid at very low pressures (1 mm.), being obtained as a crystalline solid melting at 18°. The commercial product is a colourless viscid liquid of strongly acidic taste, and contains water. Heating under ordinary pressure with the object of removing water causes partial conversion into different anhydrides (180) even before dehydration is complete, as can be detected by the diminution of the acid-equivalent indicated by titration.

Lactates.—The potassium and sodium salts are very soluble in water, solutions of 45 per cent. strength having the consistence of glycerol, and often being employed as a substitute for it. Zinc lactate forms well-developed crystals with three molecules of water. A characteristic, complex sodium ferric lactate soluble with difficulty in cold water has the composition $Fe(C_3H_4O_3)_2Na,2H_2O$, and separates in small, almost colourless leaflets on evaporation of a solution of sodium lactate and ferric chloride.

The constitution of lactic acid is inferred from its formation from acetaldehyde by the cyanohydrin-synthesis (179, 5), and by the oxidation of propyleneglycol. Lactic acid heated alone or with dilute sulphuric acid yields acetaldehyde and formic acid:

$$CH_3\cdot CHO\boxed{H\cdot COOH} \rightarrow CH_3\cdot C\overset{H}{\underset{O}{}} + H\cdot COOH.$$

This decomposition may be regarded as a reversal of the cyanohydrin-synthesis, and is characteristic of many 1-hydroxy-acids.

Lactic acid, $CH_3\cdot\overset{H}{\underset{OH}{C}}\cdot COOH$, contains one asymmetric carbon atom.

In accordance with the principles laid down in 48, it ought to exist in three isomeric modifications, and all are known. Ordinary lactic acid obtained by synthesis is *racemic*, consisting of the dextro-acid and lævo-acid in equal proportion, and therefore being optically inactive. Dextrolactic acid and lævolactic acid can be obtained from the inactive modification by methods described in 195. The dextrorotatory variety is a constituent of meat-juices, and therefore sometimes is called "sarcolactic acid."

183. The synthetic lactic acid is inactive, and hitherto optically active products have not been prepared from inactive substances by wholly chemical means. Since the inactive modification consists of equal parts of dextrorotatory and lævorotatory substance, both must be formed in the synthesis in equal proportion. An explanation of this phenomenon is afforded by a consideration of the following examples.

The nitrile of lactic acid is obtained by the addition of hydrogen cyanide to acetaldehyde (179, 5), the structural formula of this aldehyde being represented in Fig. 43:

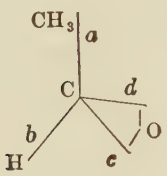


Fig. 43.
Acetaldehyde.

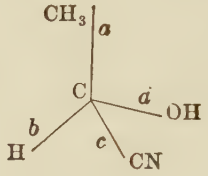


Fig. 44.
Lactonitrile.

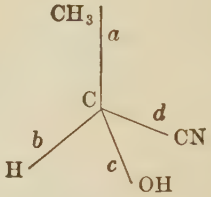


Fig. 45.
Lactonitrile.

The addition of hydrogen cyanide can take place in two ways, the oxygen doubly united with the central carbon atom of the figure becoming severed either from the bond *c* or from *d*. In the first type the cyano-group becomes attached to *c* (Fig. 44), and a hydroxyl-group is formed at *d*; and in the second type this arrangement is reversed (Fig. 45). The configurations obtained are mirror-images, cannot be made to coincide, and represent asymmetric carbon atoms.

The possibility of the formation of both active components is evident, and the inevitability of their production in equal proportion is made clear by a consideration of the *probability* of their formation. It is alike for both, *d* and *c* occupying similar positions with respect to *a* and *b*, and there being no tendency for the oxygen to remain attached to the one more than to the other.

In this example an asymmetric carbon atom has resulted from an *addition*-reaction. An example of the formation by *substitution* of a compound containing such an atom is that of 1-bromopropionic acid, $\frac{Br}{H}>C<\frac{CH_3}{COOH}$, from propionic acid, $\frac{cH}{dH}>C<\frac{CH_3}{COOH}$. By replacement of Hc and H*d* respectively, two acids of opposite rotation are produced, the probability of the formation of one being equal to that of the formation of the other.

Compounds containing an asymmetric carbon atom can be produced also through the elimination of a group, as in the formation of methyl-

ethylacetic acid, $\begin{matrix}CH_3\\C_2H_5\end{matrix}>C<\begin{matrix}H\\COOH\end{matrix}$, from methylethylmalonic acid, $\begin{matrix}CH_3\\C_2H_5\end{matrix}>C<\begin{matrix}\overset{c}{COOH}\\\underset{d}{COOH}\end{matrix}$, by loss of carbon dioxide. The probability of rupture at *c* is equal to that of its occurrence at *d*, an inactive mixture being formed.

184. Vigorous heating of optically active lactic acids and of other optically active substances converts each into the corresponding optically inactive form, containing equal proportions of the dextro-modification and the lævo-modification, the process involving the conversion of one-half of the optically active substance into its optical isomeride.

Sometimes optical inactivity is attained without the aid of heat. With the dextrorotatory *iso*butyl bromopropionate, $CH_3 \cdot CHBr \cdot COOC_4H_9$, and with other compounds having a bromine atom in union with an asymmetric carbon atom, WALDEN noted the development of optical inactivity as a result of maintenance for three or four years at the ordinary temperature. Under such conditions, the velocity of transformation of these compounds is measurable, but for most substances it is too small to be appreciable after the lapse of even long periods, and is measurable only at elevated temperatures, which accelerate most reactions.

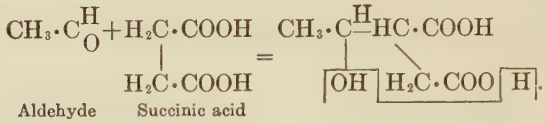
Lactones.

185. The 3-hydroxy-acids lose water very readily, with formation of *lactones* (176 and 180). This tendency with some 3-hydroxy-acids is so marked as to cause liberation from their salts, followed instantly by elimination of one molecule of water and the formation of a lactone. This phenomenon is another example of the ready generation of ring-compounds with four carbon atoms (167). Many 3-hydroxy-acids are unknown in the free state, and exist only in the form of esters, salts, or amides. The lactones are stable towards an aqueous solution of sodium carbonate, but are converted by the hydroxides of the alkali-metals into salts of 3-hydroxy-acids, a reaction proving their constitution. They can be regarded as the inner esters of the hydroxy-acids.

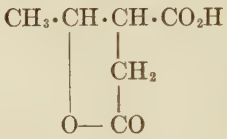
The lactones can be prepared by several methods, exemplified by the ready conversion into lactones of acids containing a double bond at the 2-position or 3-position (Δ^2 acids or Δ^3 acids) by warming with dilute sulphuric acid. This formation of lactones can be considered to involve an addition of the carboxyl-group at the double bond:

$$R\cdot\overset{3}{C}H:\overset{2}{C}H\cdot\overset{1}{C}H_2\cdot\underset{H\cdot O}{\underset{|}{CO}} \rightarrow R\cdot\underset{\rlap{\_\_\_\_\_}|}{CH}\cdot CH_2\cdot CH_2\cdot\underset{\rlap{\_\_\_\_\_}|}{CO}\ .$$

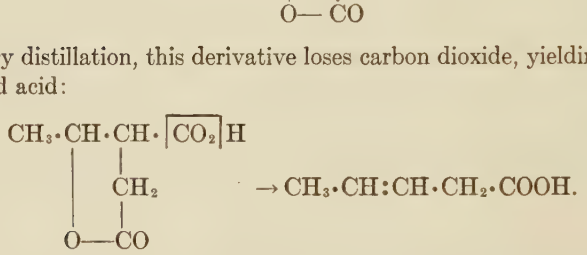
Unsaturated Δ^2-acids can be obtained by several methods, one being the action of aldehydes on sodium succinate in presence of acetic anhydride:



Elimination of one molecule of water produces a lactonic acid,

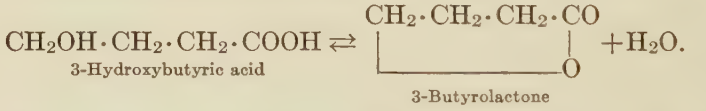


On dry distillation, this derivative loses carbon dioxide, yielding the unsaturated acid:



Another method for the preparation of lactones is the reduction of 3-ketonic acids (233, 3). 4-Lactones and 5-lactones also are known.

186. Boiling with water converts the lactones partly into the corresponding hydroxy-acids, the proportion of acid formed being in a measure dependent on that of the water present. An equilibrium between the system *acid and lactone+water* is attained:



If the molecular concentration per litre of the 3-hydroxybutyric acid be A, and if, after the lapse of a time t, x molecules have been converted into lactone, the velocity of lactone-formation s at that instant is given by the equation

$$s = k(A - x),$$

k being the reaction-constant. Simultaneously the converse reaction also occurs, the acid being regenerated from the lactone and water. With the lactone dissolved in a large excess of water, no appreciable error is introduced by assuming the quantity of the solvent to be constant. Under such conditions the velocity s' of this converse reaction is represented by the equation

$$s' = k'x,$$

k' again being the reaction-constant. The total velocity of the lactone-formation for each instant is equal to the difference between these velocities:

$$s - s' = \frac{dx}{dt} = k(A - x) - k'x. \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

For equilibrium, $s = s'$, and substitution of x_1 for the value of x at this point gives

$$k(A - x_1) - k'x_1 = 0, \quad \text{or} \quad \frac{k}{k'} = \frac{x_1}{A - x_1}. \quad . \quad . \quad . \quad . \quad (2)$$

Equations 1 and 2 can be solved for k and k'. The same method of calculation is applicable to ester-formation from an acid and an alcohol, and furnishes a mode of computing the reaction-constant of the ester-formation, and that of the ester-decomposition.

The lactones form addition-products with hydrogen bromide as well as with water, yielding 3-bromo-acids, their constitution being inferred from their reconversion into the parent substances (**176**). The lactones also give addition-products with ammonia, generating the amides of the 3-hydroxy-acids.

III. DIBASIC HYDROXY-ACIDS.

187. The simplest *dibasic hydroxy-acid* is *tartronic acid*,

$$COOH \cdot CHOH \cdot COOH.$$

It can be obtained by the oxidation of glyceric acid,

$$CH_2OH \cdot CHOH \cdot COOH,$$

with nitric acid, and is a crystalline solid melting at 187° with evolution of carbon dioxide. The glycollic acid, $CH_2OH \cdot COOH$, formed yields a polymeride of glycollide (**181**) by instant elimination of water.

A substance of greater importance is *malic acid*, $C_4H_6O_5$, present in various immature fruits, the most suitable source being unripe mountain-ash berries. It is a crystalline solid melting at 100°, and is soluble readily in water and in alcohol. Natural malic acid is optically active.

It is possible in several ways to prove malic acid to be hydroxy-succinic acid, $COOH \cdot CHOH \cdot CH_2 \cdot COOH$. Among them are its reduction to succinic acid by heating with hydrogen iodide, its conversion into monochlorosuccinic acid by the action of phosphorus pentachloride, and so on. Its alcoholic character is indicated by the formation of an acetate through the interaction of its diethyl ester and acetyl chloride.

The conversion under the influence of heat of malic acid into fumaric acid and maleic acid has been mentioned (169). In addition to the natural lævorotatory acid, both a dextrorotatory and an inactive modification are known. The inactive form can be resolved by fractional crystallization of its cinchonine salt into its two optically active components. As indicated by its structural formula, malic acid contains an asymmetric carbon atom.

Ethane-1:2-diol-1:2-dicarboxylic or Tartaric Acids, $C_4H_6O_6$.

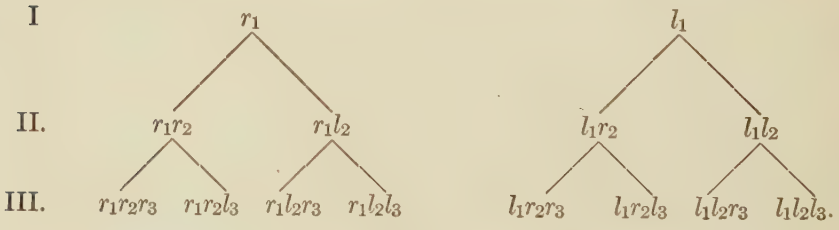
188. Four acids of the composition $C_4H_6O_6$ are known, each with the constitutional formula

$$COOH \cdot CHOH \cdot CHOH \cdot COOH.$$

They are termed *dextrorotatory tartaric acid, lævorotatory tartaric acid, racemic acid,* and *mesotartaric acid,* the last two being optically inactive. Their constitution is proved by their formation by boiling the silver salts of the dibromosuccinic acids with water, these acids being obtained from fumaric acid or maleic acid by the action of bromine. It is indicated also by their production from glyoxal (198) by the cyanohydrin synthesis. The inactive modifications are produced by these reactions (183).

In accordance with their constitutional formula, the tartaric acids contain two asymmetric carbon atoms in the molecule, and it is necessary to consider the number of stereoisomerides theoretically possible.

While a single asymmetric carbon atom there are two optical isomerides, r_1 and l_1 (I). Addition of a second asymmetric carbon atom, either dextrorotatory or lævorotatory, produces the combinations II of the subjoined scheme. Increase in the number of carbon atoms to three gives similarly eight isomerides (III). Obviously for n asymmetric carbon atoms the number of possible isomerides is 2^n.



In this scheme all the asymmetric carbon atoms are assumed to be dissimilar, and the racemic combinations are left out of consideration.

Since tartaric acid contains two *similar* asymmetric carbon atoms, or asymmetric carbon atoms in union with similar groups, l_1r_2 and l_2r_1 become identical, leaving so far three isomerides possible. r_1r_2 and l_1l_2 being able to unite to form a racemic compound, the total number of possible isomerides is raised to four:

	1	2	3	4
CH(OH)(COOH)	Dextro	Dextro	Lævo	Inactive combination of r_1r_2 and l_1l_2
CH(OH)(COOH)	Dextro	Lævo	Lævo	

The four tartaric acids, $C_4H_6O_6$, correspond in properties with the four isomerides theoretically possible. Dextrotartaric acid and lævotartaric acid must be represented respectively by 1 and 3, since in these schemes each carbon atom rotates the plane of polarization in the same direction, and therefore each should reinforce the influence of the other. The optically inactive mesotartaric acid is represented by 2. Its two asymmetric carbon atoms rotate the plane of polarization equally, but in opposite directions, and thus each neutralizes the effect of the other. Finally, isomeride 4 is racemic acid.

An important difference exists between the two optically inactive isomerides, racemic acid and mesotartaric acid. The first is obtained by mixing equal quantities of the dextro-acid and the lævo-acid, and can be resolved into its components. The second consists of one kind of molecules only, and cannot be resolved. The rotation caused by the dextro-acid is equal in amount but opposite in sign to that due to the lævo-acid.

189. Emil Fischer has introduced a simple mode of writing the spacial formulæ of optically active compounds, frequently employed in

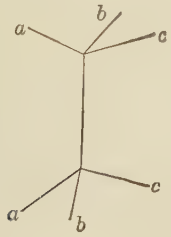


Fig. 46.

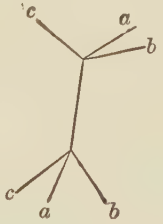
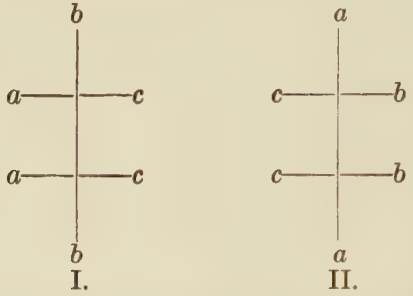


Fig. 47.

the sequel. The representation in space of two carbon atoms in union in a compound $\begin{matrix} Cabc \\ | \\ Cabc \end{matrix}$ is shown in Fig. 46 (**167**).

If the two bonds uniting the two carbon atoms be supposed to lie

in the plane of the paper, the positions of *a* and *c* are at the back, and that of *b* at the front. If *a*, *b*, and *c* be imagined to be projected upon the plane of the paper, and *a* and *c* simultaneously to be altered in position so as to lie in the same straight line at right angles to the vertical axis, and if *b* lie in the production of this axis, projection-figure I is obtained:

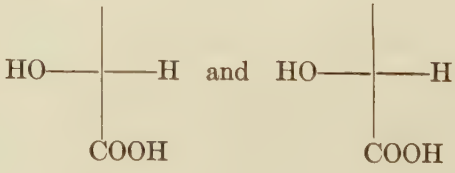


If Fig. 46 be rotated its vertical axis, so as to bring *a* in front of the plane of the paper, Fig. 47 results, its projection being represented by II. These apparently different configurations are identical.

For a chain of four carbon atoms there is obtained analogously the projection-figure

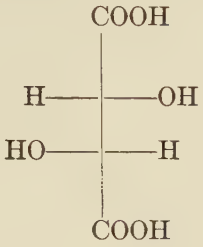
This mode of representation will be understood by imagining the figures in **167** (Fig. 31) to be placed so as to bring the plane of the carbon bonds at right angles to that of the paper, and the figures in this position to be projected in the manner described.

190. The projection-formulæ for the four isomeric tartaric acids are obtained by the following procedure. If the projection-figure for two asymmetric carbon atoms be divided in the middle of the vertical line, and the upper half of the figure rotated through 180° in the plane of the paper, the similar grouping of HO, H, and COOH about the asymmetric carbon atoms in the halves



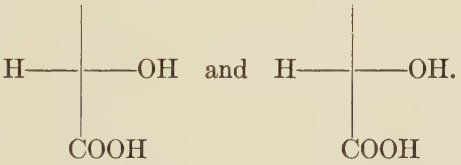
indicates both carbon atoms to rotate the plane of polarization in the same direction. This grouping will be assumed arbitrarily to occasion dextrorotation.

When the two carbon atoms are reunited by transposing one of the halves in the plane of the paper, the figure

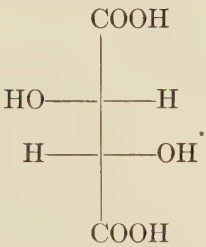


is obtained, and is therefore the projection-formula for the dextrorotatory acid.

The grouping with respect to the two carbon atoms in the lævorotatory acid must be the mirror-image of that in the dextrorotatory isomeride (48), in accordance with the scheme



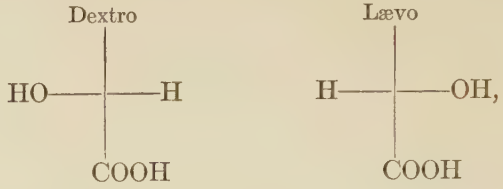
The combination of these two gives for the lævorotatory acid the projection-formula



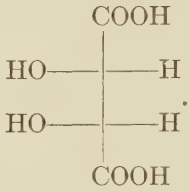
These representations of the constitutions of dextrotartaric acid and lævotartaric acid cannot be made to coincide by altering their positions in the plane of the paper,* and are therefore different.

* These projection-formulæ can be made to coincide by rotating one of them through 180° about the line HO—H. From a model the impossibility of making the *spacial* formulæ coincide by this means can be seen. To determine by means of projection-formulæ the possibility of coincidence for the corresponding spacial formulæ, it is only admissible to transpose the projections in the plane of the paper.

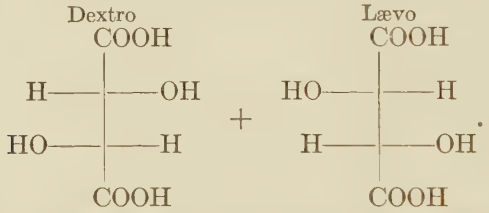
When the acid contains a dextrorotatory carbon atom and a lævorotatory carbon atom, as in mesotartaric acid, the arrangement of the groups is



and their projection-formula is



The projection-formula for racemic acid is



It has been possible to demonstrate the dextrorotatory acid and the lævorotatory acid to have the configurations indicated by the projection-formulæ, and not the converse structures, but the proof is beyond the scope of this book.

Dextrotartaric Acid.

191. *Potassium hydrogen* d-*tartrate*, $C_4H_5O_6K$, is present in the juice of grapes, and during alcoholic fermentation is deposited on the bottom of the casks, being even more sparingly soluble in dilute alcohol than in water. The crude product is termed "Argol," and the purified salt is known as "Cream of tartar." To obtain *dextrotartaric acid*, argol is boiled with hydrochloric acid, and the acid is precipitated with milk of lime as calcium tartrate, $CaC_4H_4O_6$. After washing, the calcium salt is decomposed by an equivalent quantity of sulphuric acid, calcium sulphate being precipitated and the tartaric acid liberated. The free acid can be obtained by evaporation in the form of large transparent crystals without water of crystallization, and having the composition $C_4H_6O_6$.

Dextrotartaric acid melts at 170°. It is soluble in water very

readily, to a less extent in alcohol, and is insoluble in ether. Heating above its melting-point at atmospheric pressure eliminates water and yields various anhydrides, their identity depending on the intensity and duration of the process. Stronger heating turns it brown, with production of a caramel-like odour. A still higher temperature causes charring, with formation of pyruvic acid (**231**) and pyrotartaric acid, $COOH \cdot CH(CH_3) \cdot CH_2 \cdot COOH$. It can be converted into succinic acid by the action of certain bacteria.

In addition to the potassium hydrogen tartrate may be mentioned the *normal potassium salt*, $C_4H_4O_6K_2$, readily soluble in water, and *potassium antimonyl tartrate*,

$$2[COOK \cdot CHOH \cdot CHOH \cdot COO(SbO)] + H_2O.$$

On account of its medicinal properties the antimony derivative is known as "Tartar emetic." It is obtained by boiling potassium hydrogen tartrate with antimony oxide and water, and dissolves readily in water.

The precipitation of hydroxides from metallic salts, exemplified by that of cupric hydroxide from cupric sulphate, is prevented (**157**) by the presence of tartaric acid. The liquid obtained by dissolving cupric sulphate, tartaric acid, and excess of potassium hydroxide in water is termed "Fehling's solution." It is an important means of testing the reducing power of compounds, since reducers precipitate yellowish-red cuprous oxide or its hydroxide from the dark-blue solution. In this alkaline copper solution the hydroxyl-groups of the central carbon atoms react with the cupric hydroxide, since one gramme-molecule of normal alkali tartrate can dissolve one gramme-molecule of cupric hydroxide. These cupric alkali tartrates have been obtained also in crystalline form, the compound $C_4H_2O_6Na_2Cu,2H_2O$ being known, and having the constitutional formula

$$Cu\begin{<}{O \cdot CH \cdot COONa \atop O \cdot CH \cdot COONa}\end{>} + 2H_2O.$$

Experiment has proved this compound in aqueous solution to be ionized to $Na^{\cdot}$ and the complex anion $Cu\begin{<}{O \cdot CH \cdot COO' \atop O \cdot CH \cdot COO'}\end{>}$. The solution is found to lack the reactions characteristic of copper ions, and although it is alkaline cupric hydroxide is not precipitated. On electrolysis the copper tends towards the anode. This phenomenon has been studied by Küster by the aid of the apparatus shown in Fig. 48. One U-tube contains cupric-sulphate solution at *b*; the other, Fehling's solution at *d*. Into both limbs of each is poured carefully a solution of sodium sulphate, *a* and *c*. The common surfaces of the sodium-sulphate and cupric-sulphate solutions in the two U-tubes lie in the same horizontal plane. When an electric

current is passed through the tubes, preferably arranged in parallel and not in series, a different effect is produced on the level of the surfaces of the copper solutions in each tube. In the cupric-sulphate solution there is a rise at the cathode, the cupric ions being cations and tending towards that electrode. The converse effect is observed in the FEHLING'S solution, indicating the copper in it to be a constituent of the anion. The arrows in the figure show the direction tendency of the ions in each solution.

The colour of FEHLING'S solution is also a much more intense blue than that of a cupric-sulphate solution of equivalent concentration, evidence of the presence in FEHLING'S solution of a complex ion containing copper.

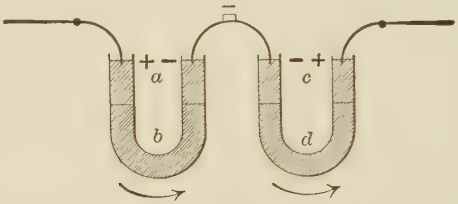


FIG. 48.—ELECTROLYSIS OF AN ALKALINE COPPER SOLUTION.

FEHLING'S solution decomposes gradually, and it is best to prepare it as required. OST discovered a much more stable alkaline copper solution, applicable to the same purposes as that of FEHLING. It is a mixture of cupric sulphate with potassium hydrogen carbonate and potassium carbonate, and contains a soluble double carbonate of copper and potassium.

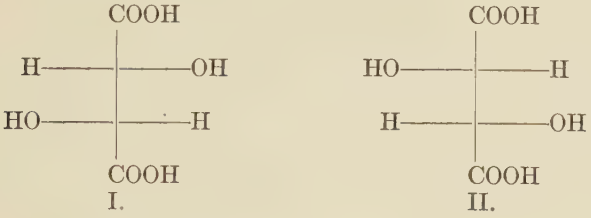
Laevotartaric Acid.

Lævotartaric acid is obtained from racemic acid. With two exceptions, the properties of the lævo-acid and its salts are identical with those of the dextro-modification and its salts. First, their rotatory power is equal, but opposite in sign; second, the salts formed by the lævo-acid with the optically active alkaloids differ in solubility from those derived from the dextro-acid (195).

Racemic Acid.

192. Optically active substances are stated in 184 to be converted by the action of heat into optically inactive compounds, being changed into a mixture of the dextro-modification and the lævo-modification in equal proportion. This change is facilitated often by the presence of certain substances, dextrotartaric acid being converted readily into *racemic acid* by boiling with excess of a concentrated solution of sodium hydroxide. Mesotartaric acid is formed simultaneously (193).

The optical inactivity is occasioned by conversion of one-half of the dextro-acid into the lævo-modification. If formula I represent the dextro-acid, then formula II will correspond with the lævo-acid; and the formulæ indicate it to be essential for the exchange of groups causing the conversion of an active compound into its optical isomeride (184) to occur in this instance at both asymmetric carbon atoms, to enable the dextro-acid to yield its lævo-isomeride:



Racemic acid is not so soluble in water as the two optically active acids; and it differs in crystalline form from them, the crystals having the composition $2C_4H_6O_6,2H_2O$. In many of its salts the proportion of water of crystallization differs from that in the corresponding optically active salts. Racemic acid is proved to consist of two components by its synthesis from solutions of the dextro-acid and the lævo-acid. With concentrated solutions heat is developed by mixing, and the less soluble racemic acid crystallizes. Racemic acid also can be resolved into the two optically active modifications (195).

Although racemic acid in the solid state differs from both dextrotartaric acid and lævotartaric acid, yet in solution or as ester in the state of vapour it is only a mixture of them. The cryoscopic depression produced by it corresponds with the molecular formula $C_4H_6O_6$, and the vapour-density of its ester with single and not double molecules.

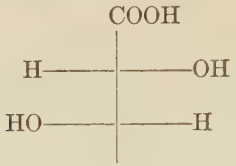
The term "racemic" is applied to substances consisting of isomerides of equal and opposite rotatory power in equimolecular proportions, and therefore optically inactive. This phenomenon was observed first by Pasteur in his researches on racemic acid (195).

Mesotartaric Acid.

193. Like racemic acid, *mesotartaric acid* is optically inactive, but cannot be resolved into optically active components. It is formed by boiling dextrotartaric acid for several hours under a reflux-condenser with a large excess of sodium hydroxide (192).

If formula I be assigned to dextrotartaric acid, obviously to convert it into mesotartaric acid with formula II, it is necessary only for two groups

in union with a single asymmetric carbon atom to change places, while racemic acid can be formed only through exchange of the groups attached to



I.

II.

both carbon atoms. This view affords an explanation of the initial formation of mesotartaric acid by heating dextrotartaric acid with dilute hydro-

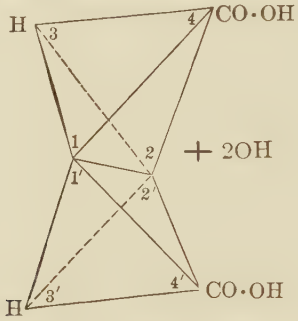


Fig. 49.—Maleic Acid.

chloric acid, or by boiling it with dilute sodium hydroxide, racemic acid being produced only by prolonged heating.

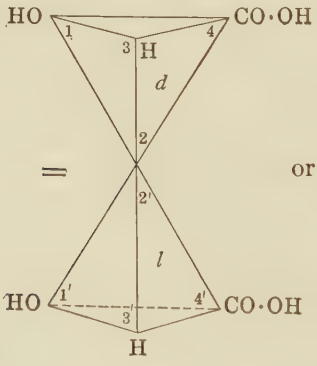


Fig. 50.—Mesotartaric Acid.

or

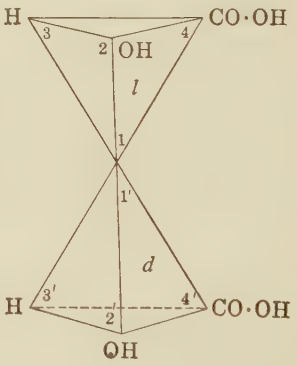
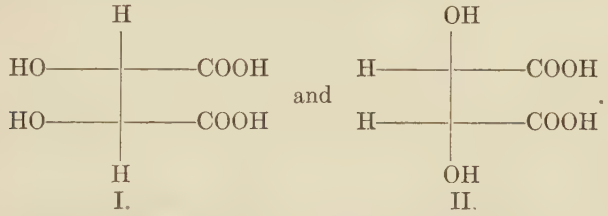


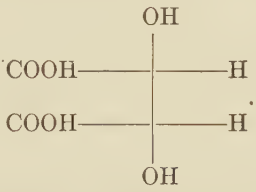
Fig. 51.—Mesotartaric Acid.

Potassium hydrogen mesotartrate dissolves readily in cold water, differing in this respect from the corresponding salts of the other tartaric acids.

194. This view of the structure of the tartaric acids is in complete accord with their relation to fumaric acid and maleic acid (169). Almost quantitative yields of racemic acid and mesotartaric acid can be obtained by oxidizing fumaric acid and maleic acid in aqueous solution by means of potassium chlorate in presence of osmium tetroxide, OsO_4, as catalyst, two hydroxyl-groups being added. The process converts fumaric acid into racemic acid, and maleic acid into mesotartaric acid. Addition of two hydroxyl-groups to maleic acid may result from the rupture of the bond 1:1′ or 2:2′ in Fig. 49, with production of the configurations represented in Figs. 50 and 51. The projection-formulæ corresponding with Figs. 50 and 51 are



These apparently different configurations are identical, as becomes evident on rearranging I (189):



If the last projection-formula be rotated in the plane of the paper through 180°, it will coincide with II. A comparison of this scheme with that in 193 shows it to be the configuration representing mesotartaric acid, indicating addition of two hydroxyl-groups to maleic acid to produce mesotartaric acid only.

A different result is obtained by addition of two hydroxyl-groups to fumaric acid, as is demonstrated by Figs. 52 and 53:

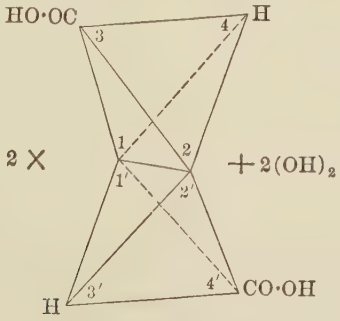


Fig. 52.—Fumaric Acid.

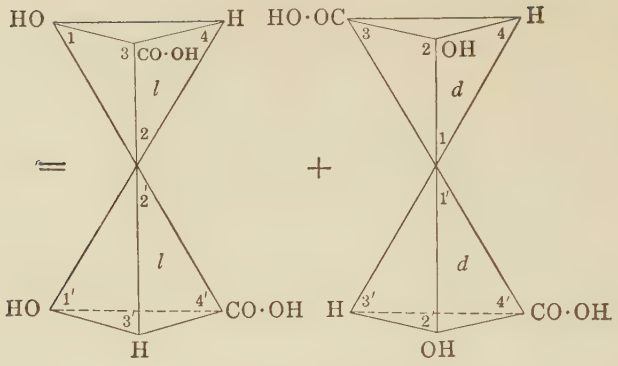
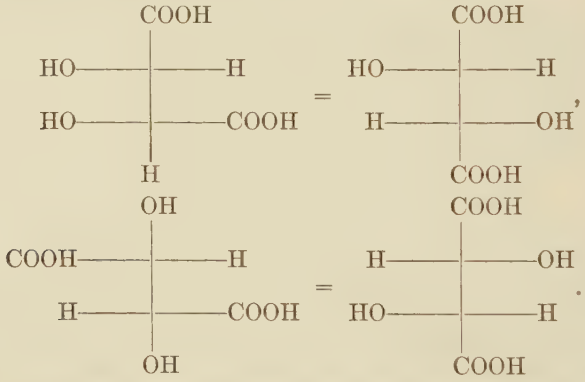


Fig. 53.—Racemic Acid.

Severance of the bonds 1:1′ or 2:2′ by addition yields two configurations incapable of being made to coincide by rotation. This fact is made clearer by the projection-formulæ



These projection-formulæ are identical with the configurations representing dextrotartaric acid and lævotartaric acid (**190**).

The addition of chlorine to the neutral salts of fumaric acid and maleic acid dissolved in a saturated solution of sodium chloride is quite analogous. Maleic acid yields 1:2-*dichloroethanedicarboxylic acid*-1:2, the meso-form of dichlorosuccinic acid; and fumaric acid gives the racemic form of iso-*dichlorosuccinic acid.*

Racemic Substances, and their Resolution into Optically Active Constituents.

195. Optically active isomerides display no difference in their physical properties or in their chemical properties, except the rotation of the plane of polarized light in opposite directions, and certain physiological effects not yet explained. Accordingly they have the same solubility, boiling-point, and melting-point; their salts crystallize with the same number of molecules of water of crystallization; and so on. Hence the

resolution of an optically inactive substance into its optically active components cannot be effected by the ordinary methods, for they are based on differences in physical properties.

Pasteur devised three methods for effecting this resolution. The first process depends on the fact of racemates sometimes crystallizing from solution in two forms, one corresponding with the dextro-salt, and the other with the lævo-salt. These products can be separated mechanically. Pasteur effected this partition for sodium ammonium racemate, $C_8H_8O_{12}Na_2(NH_4)_2,2H_2O$. Crystals of the dextrotartrate and of the lævotartrate are obtained from its solution only at temperatures below 28°, the transition-point for these salts ("Inorganic Chemistry," 70):

$$2Na(NH_4)C_4H_4O_6,4H_2O \rightleftarrows C_8H_8O_{12}Na_2(NH_4)_2,2H_2O+6H_2O.$$

Dextro-+lævo-sodium ammonium tartrate — Sodium ammonium racemate

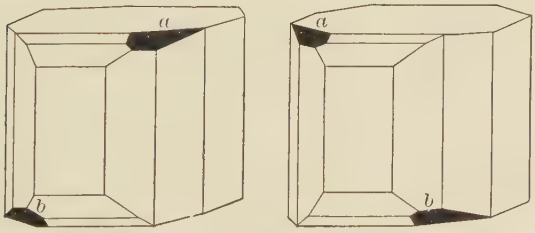


Fig. 54.—Crystal-forms of the Sodium Ammonium Tartrates.

Fig. 54 represents the crystal-forms of the two tartrates, the difference between them being due to the positions of the planes *a* and *b*. The crystal-forms are mirror-images, and cannot be made to coincide.

The separation of these two forms is effected by careful evaporation of a solution of the sodium ammonium racemate on a water-bath until a certain density has been attained, it being then allowed to cool slowly so as to become supersaturated. A crystal of a dextrorotatory salt and one of a lævorotatory salt are placed some distance apart in the liquid. On the following day each of these nuclei will be found to be surrounded by a thick mass of crystals having a rotatory power similar in kind to that of the parent nucleus. If no crystal is available for the purpose of this inoculation, the assistance of an isomeric substance may be requisitioned, this process being exemplified by the crystallization of the *d*-tartrate through addition of a crystal of *l*-asparagine to the solution, the *l*-tartrate remaining dissolved.

This method of separation can be employed very rarely. It has also been applied by Purdie to the resolution of racemic lactic acid, almost

instantaneous crystallization being induced by the inoculation of a saturated solution of racemic ammonium zinc lactate

$$Zn(C_3H_5O_3)_2,NH_4C_3H_5O_3,2H_2O,$$

with the corresponding dextrorotatory or lævorotatory salt.

Pasteur's second method of resolution depends on a difference in solubility of the salts formed by uniting optically active acids with optically active bases. On union of a dextro-acid or a lævo-acid with an optically inactive base, as in the metallic salts, the internal structure of the molecule remains unchanged; and the constitution of the salt-molecules, like that of the free acids, can be represented by mirror-image configurations. It is otherwise for the combination of the dextro-acid and the lævo-acid with an optically active base, either dextrorotatory or lævorotatory, the configurations of the salt-molecules being mirror-images no longer, and identity of physical properties ceasing of necessity.

In this manner racemic acid can be resolved by means of its cinchonine salt, cinchonine lævotartrate being less soluble than the dextrotartrate, and crystallizing from solution first. Strychnine can be employed advantageously in the resolution of lactic acid, and other similar examples might be cited.

The conversion of enantiomorphic isomerides into derivatives with configurations no longer mirror-images of one another can be effected otherwise, a mode for acids being the formation of an ester with an optically active alcohol. On account of the perfectly symmetrical structure of the esters formed, the velocity of ester-formation with an optically inactive alcohol must be the same for both isomerides; but with an optically active alcohol the two isomerides are not esterified at the same rate, the compounds produced being no longer mirror-images. Marckwald found that heating racemic mandelic acid (324) for one hour at 155° with the active alcohol menthol (365), leaves the lævorotatory acid unesterified.

The third method of fission devised by Pasteur depends on the action of mould-fungi (*Penicillium glaucum*) or of bacteria. Contact of racemic lactic acid in very dilute solution with the *Bacillus acidi lævolactici*, in presence of the necessary nutriment for the bacteria, renders the optically inactive solution lævorotatory, only the dextrorotatory acid being converted by the bacilli into other substances. A dilute solution of racemic acid containing traces of the mould-fungus *Penicillium glaucum* becomes lævorotatory, the fungus propagating through decomposition of the dextrorotatory acid.

The second and third methods of resolution are alike in principle. During their growth the bacteria and fungi develop substances termed enzymes (222), and able to decompose compounds by means hitherto unexplained. These enzymes are optically active, and obviously a difference in their action on the optical isomerides analogous to that described in the previous paragraph is to be expected.

A liquid or gaseous racemic substance consists only of a mixture of the two enantiomorphic isomerides, an example being afforded by racemic acid in solution and in the form of esters (192). For crystalline substances there are three possibilities.

First, the individual crystals may be dextrorotatory or lævorotatory, the two modifications being separable mechanically. In this instance the racemic substance is said to be a *conglomerate* of the isomerides.

Second, the substance may be a true compound of the dextro-modification and the lævo-modification, a *racemic* compound or *racemoid*, its formation being comparable with that of a double salt, formed by the crystallization under certain conditions of a solution containing two salts.

The third possibility also is analogous to the crystallization of salt-solutions, whereby sometimes crystals containing both salts are obtained, but in proportions varying in different crystals. Sometimes the salts crystallize together in all proportions, but usually the ratio can vary between certain limits only. This simultaneous crystallization of salts yields the so-called *mixed crystals*, and optical isomerides produce pseudo*racemic* mixed crystals.

The variety of crystals obtained from a given solution or fused mass of a racemic substance—a conglomerate, a racemic compound, or *pseudo*racemic mixed crystals—depends on the temperature of crystallization and other conditions. An example of this relationship is afforded by sodium ammonium racemate. On concentration above 28° the racemate crystallizes from the solution of this salt; below this temperature a mixture of the individual tartrates or conglomerate is obtained.

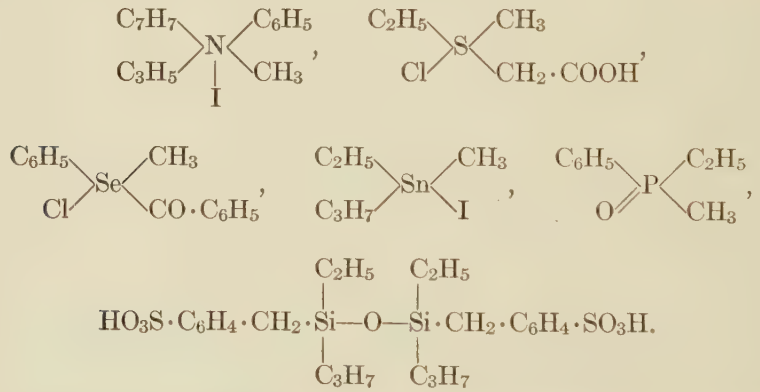
Bakhuis Roozeboom indicated a method of distinguishing these three classes of compounds. For a conglomerate the procedure is simple. An optically inactive solution saturated alike for the dextrorotatory form and for the lævorotatory body is made. Adding the solid dextro-compound or lævo-compound and agitating the mixture does not effect further solution, the liquid being saturated already with respect to the two isomerides. The amount of dissolved substance is still the same, and the solution remains optically inactive. In presence of a racemic compound, the solution is saturated initially

by it, but unsaturated with respect to the two optically active modifications; addition of the solid dextrorotatory or lævorotatory substance causes a change in the total quantity of solid dissolved, and the liquid becomes optically active. Sometimes less simple methods are necessary to detect *pseudo*racemic mixed crystals.

Optically Active Compounds with Asymmetric Atoms Other than Carbon.

196. The methods of separation outlined in **195** have made possible also the resolution into optical isomerides of other compounds of asymmetric structure, a result in accord with Pasteur's principle of the "Dissymmétrie moléculaire" (**48**). The presence of an n-valent atom of any kind in union with n dissimilar substituents always necessitates a structure capable of existence in two configurations, mirror-images of each other, but not superimposable.

By employing the highly rotatory *d*-bromocamphorsulphonic acid and its lævo-isomeride it is possible to resolve into their optical components basic substances of the types indicated. Substitution of acetone or some other solvent for water in the fractional crystallization of the salts prevents hydrolytic dissociation. Optically active compounds with asymmetric nitrogen, sulphur, selenium, tin, phosphorus, and silicon atoms are known, examples being



As a general rule, an asymmetric molecular structure induces optical activity, and the fine researches of Werner on asymmetric metallic atoms furnished additional evidence in support of this statement. In the complex derivatives of cobalt, chromium, iron, and other metals, Werner assumed ("Inorganic Chemistry," **330**) the presence

of six atoms or groups in direct union with the metallic atom, these groups being supposed to be situated at the angles of a regular octahedron with the metallic atom at its centre. Two groupings are possible for compounds of the type $Me^{*}\begin{matrix}A_2\\B_4\end{matrix}$, as indicated in Figs. 55 and 56, resulting either from "Axial-substitution" (Fig. 55), or from "Edge-substitution" (Fig. 56). The possibility of the existence of two stereoisomerides is made evident, and many examples of this type of isomerism are known. The possibility of the existence in two stereoisomeric forms of compounds $Me\begin{matrix}A_3\\B_3\end{matrix}$ is also clear.

Fig. 55.

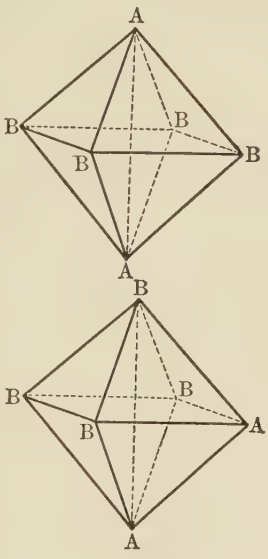


Fig. 57.

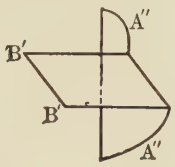


Fig. 56.

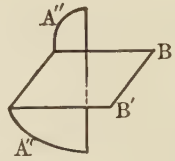


Fig. 58.

Figs. 55, 56, 57, and 58.—Werner's Theory of Stereoisomerism.

As a basis for assigning to a compound MeA_2B_4 the configuration represented in Fig. 55 or that in Fig. 56, Werner made the very plausible assumption of the union of a bivalent group, such as ethylenediamine, carbon dioxide, or oxalic acid, being possible only through edge-substitution. In accordance with this view, exchange of the carbon dioxide or other bivalent group for two univalent groups must produce compounds also with the configuration of Fig. 56.

Since both stereoisomerides have a plane of symmetry, optical activity is impossible for compounds MeA_2B_4 with univalent groups A and B. An octahedral arrangement around the metallic atom of a bivalent group and two univalent groups, or of three bivalent groups, makes possible the existence of two non-superimposable forms without a plane of symmetry (Figs. 57 and 58), and some compounds of this type have been resolved into their optical antipodes. Often they are characterized by a very high specific rotatory power, that of a complex iron derivative of the tri-α-dipyridyl-ferrous series being about 500°.

* Me represents a metallic atom.

IV. POLYBASIC HYDROXY-ACIDS.

197. Of these acids it will be sufficient to describe the tribasic *citric acid*, $C_6H_8O_7$, a substance distributed widely in the vegetable kingdom, and present also in cows' milk to the extent of 0·1 per cent. It is prepared from the juice of unripe lemons, their content being between 6 and 7 per cent. Tricalcium citrate dissolves readily in cold water, but very slightly in boiling water, a property employed in the separation of the acid from lemon-juice. It is obtained in the free state by addition of sulphuric acid to the citrate. Another technical method for its preparation depends on the power of certain mould-fungi (*Citromyces pfefferianus* and *C. glaber*) to produce considerable quantities of citric acid from dextrose or sucrose, it being possible to obtain a yield up to 50 per cent.

Citric acid can be prepared synthetically by a method proving its constitution. On oxidation, symmetrical dichlorohydrin,

$$CH_2Cl\cdot CHOH\cdot CH_2Cl$$

(158), is transformed into symmetrical dichloroacetone,

$$CH_2Cl\cdot CO\cdot CH_2Cl.$$

The cyanohydrin-synthesis converts this derivative into

$$CH_2Cl\cdot C\begin{cases}OH\\CH_2Cl,\\CN\end{cases}$$

and hydrolysis yields the hydroxy-acid,

$$CH_2Cl\cdot C\begin{cases}OH\\CH_2Cl.\\COOH\end{cases}$$

With potassium cyanide this compound forms a dicyanide hydrolyzable to citric acid:

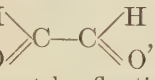
$$\begin{array}{l}CH_2\cdot CN\\|\\C<\begin{matrix}OH\\COOH\end{matrix}\\|\\CH_2\cdot CN\end{array}\rightarrow\begin{array}{l}CH_2\cdot COOH\\|\\C<\begin{matrix}OH\\COOH\end{matrix}\\|\\CH_2\cdot COOH\end{array}.$$

The alcoholic character of citric acid is indicated by the formation of an acetyl-compound from triethyl citrate and acetyl chloride.

Citric acid forms well-defined crystals containing one molecule of water of crystallization, and dissolves readily in water and alcohol. It loses its water of crystallization at 130°, and melts at 153°. It is employed in the manufacture of lemonade, and in calico-printing.

DIALDEHYDES AND DIKETONES: HALOGEN-SUBSTITUTED ALDEHYDES AND KETONES.

Dialdehydes.

198. The simplest member of the series of dialdehydes, *ethanedial* or *glyoxal*,  , is a combination of two aldehydo-groups. It is prepared best by floating a layer of water carefully on the surface of strong nitric acid contained in a tall glass cylinder, and pouring ethyl alcohol on the surface of the water, care being taken to prevent mixing of the layers. The nitric acid and alcohol diffuse into the water; and the alcohol is oxidized slowly to glyoxal, glycollic acid, oxalic acid, and other substances.

The interaction of ozone and acetylene also yields glyoxal, it being necessary to moderate the violence of the reaction by diluting both gases with air.

Glyoxal is a colourless, amorphous substance, and in the moist state it dissolves readily in water, but very slowly after complete drying *in vacuo* between 110° and 120°. It is a polymeride of unknown molecular weight, although its aqueous solution reacts as one containing simple molecules only. Distillation of this polymeride with phosphoric anhydride evolves an emerald-coloured gas, condensable by cooling to beautiful yellow crystals, and at a lower temperature becoming colourless. They melt at 15°, and the yellow liquid obtained boils at 51°. It is unimolecular glyoxal, and can exist as such only for a short time, traces of water polymerizing it readily. The unimolecular form is the simplest type of coloured compound, containing only carbon, hydrogen, and oxygen.

The combination of glyoxal with two molecules of sodium hydrogen sulphite, and the formation of a dioxime, prove it to be a double aldehyde. It has also the other properties peculiar to aldehydes, such as the reduction of an ammoniacal silver solution with formation of a mirror. On oxidation, it takes up two atoms of oxygen to yield oxalic

acid, being the dialdehyde of that acid. Potassium hydroxide converts glyoxal into glycollic acid in accordance with CANNIZZARO's reaction (108). This change may be explained by assuming and addition-product with water to be formed in accordance with the scheme

$$C\overset{H}{\underset{O}{}}\cdot C\overset{H}{\underset{O}{}} + H_2O = \underset{\text{Glycollic acid}}{CH_2OH\cdot COOH}.$$

Butane-1:4-*dial* or *succindialdehyde*, $C\overset{H}{\underset{O}{}}\cdot CH_2\cdot CH_2\cdot C\overset{H}{\underset{O}{}}$, was prepared by HARRIES by the action of ozone on a chloroform-solution of diallyl,

$$CH_2{:}CH\cdot CH_2{—}CH_2\cdot CH{:}CH_2.$$

A diozonide addition-product,

$$CH_2\cdot CH(O_3)\cdot CH_2{—}CH_2\cdot CH(O_3)\cdot CH_2,$$

is formed, each double bond uniting with one molecule of ozone. This diozonide is a viscous explosive liquid. Slow heating with water decomposes it, forming succindialdehyde.

HARRIES prepared several analogous ozonides, each double bond always uniting with one molecule of ozone. Water decomposes these ozonides in accordance with the scheme

$$>C(O_3)—C(O_3)< + H_2O = >CO + OC< + H_2O_2.$$

The formation of these ozonides and their decomposition by water afford an excellent method for determining the position in the molecule of double bonds. Its application to the problem of oleic acid has confirmed the formula indicated in **137**.

Diones or Diketones.

199. The diketones contain two carbonyl-groups, their properties and the methods employed in their preparation depending on the relative position of these groups. 1:2-Diketones with the group $—\overset{1}{C}O\cdot\overset{2}{C}O—$ are known, 1:3-diketones with $—\overset{1}{C}O\cdot\overset{2}{C}H_2\cdot\overset{3}{C}O—$, 1:4-diketones with $—\overset{1}{C}O\cdot\overset{2}{C}H_2\cdot\overset{3}{C}H_2\cdot\overset{4}{C}O—$, and so on.

1:2-*Diketones* cannot be obtained by the elimination of chlorine

from the acid chlorides by the aid of a metal, in accordance with the scheme

$$R\cdot CO\boxed{Cl+Na_2+Cl}OC\cdot R.$$

Their preparation is effected by the action of amyl nitrite and a small proportion of hydrochloric acid on a ketone, one of the methylene-groups being converted into C=NOH:

$$R\cdot CO\cdot C\boxed{\begin{matrix}H_2\\O\\NOH\end{matrix}}\cdot R' \rightarrow R\cdot CO\cdot C(=NOH)\cdot R'.$$

These compounds are termed iso*nitrosoketones*. Boiling with dilute sulphuric acid eliminates the oxime-group as hydroxylamine, with formation of the diketone. The *ketoaldehydes* are both ketones and aldehydes, containing the group $-CO\cdot C\langle{}^{H}_{O}$, and they also can be obtained by this method.

Butane-2:3-*dione* or *diacetyl*, $CH_3\cdot CO\cdot CO\cdot CH_3$, can be prepared from methylethylketone in the manner indicated. It is a yellow liquid of pungent, sweetish odour, is soluble in water, and has a vapour similar in colour to that of chlorine. Diacetyl boils at 88°, and at 20° has the density 0·973. Its behaviour indicates the presence of two carbonyl-groups in the molecule, exemplified by the addition of two molecules of hydrogen cyanide, the formation of a mono-oxime and a dioxime, and so on. The adjacency of the two carbonyl-groups in diacetyl is proved by its quantitative conversion into acetic acid under the influence of hydrogen peroxide:

$$\begin{matrix}CH_3\cdot CO-\\+\ OH\end{matrix}\boxed{\begin{matrix}CO\cdot CH_3\\OH\end{matrix}}\rightarrow 2CH_3\cdot CO\cdot OH.$$

200. 1:3-*Diketones* can be prepared by a condensation-method of general application discovered by Claisen and Wislicenus. Sodium ethoxide is the condensing agent. An addition-product is formed by the interaction of this substance and an ester:

$$R\cdot C\langle{}^{O}_{OC_2H_5}+{}^{Na}_{OC_2H_5}=R\cdot C\langle{}^{ONa}_{OC_2H_5}{}_{OC_2H_5}.$$

The addition-product is brought into contact with a ketone $R'\cdot CO\cdot CH_3$, two molecules of alcohol being eliminated with formation of a condensation-product:

$$R\cdot C\langle{}^{ONa}\boxed{\begin{matrix}OC_2H_5+H\\OC_2H_5+H\end{matrix}}CH\cdot CO\cdot R'=R\cdot C\langle{}^{ONa}_{CH\cdot CO\cdot R'}+2C_2H_5OH.$$

Dilute acid replaces the sodium atom of this compound by hydrogen. This operation might produce a derivative with a hydroxyl-group attached to a doubly-linked carbon atom; but usually substances of this type are unstable, the group $—\overset{OH}{\overset{|}{C}}=CH—$ changing to $—CO—CH_2—$. The principle applies in the present instance, $R\cdot\overset{OH}{\overset{|}{C}}=CH\cdot CO\cdot R'$ yielding a 1:3-diketone, $R\cdot CO—CH_2—CO\cdot R'$.

Claisen found sodamide, $Na\cdot NH_2$, to be a useful substitute for sodium ethoxide in the condensation of ketones with esters. Frequently it not only facilitates the reaction but increases the yield.

Another method for the preparation of 1:3-diketones is the action of acid chlorides on the sodium compounds of acetylene homologues:

$$\underset{\text{Sodio-}n\text{-amylacetylene}}{CH_3\cdot(CH_2)_4\cdot C\equiv C\boxed{Na+Cl}}\underset{\text{Acetyl chloride}}{OC\cdot CH_3} \rightarrow CH_3\cdot(CH_2)_4\cdot C\equiv C\cdot CO\cdot CH_3.$$

Concentrated sulphuric acid transforms this ketone by addition of the elements of water into the desired diketone:

$$\begin{array}{l} CH_3\cdot(CH_2)_4\cdot C\equiv C\cdot CO\cdot CH_3 = CH_3\cdot(CH_2)_4\cdot CO\cdot CH_2\cdot CO\cdot CH_3. \\ \qquad\qquad + \quad O \quad H_2 \end{array}$$

These diketones have a weak acidic character, their dissociation-constants being very small. Among those determined is that of *pentane-2:4-dione* or *acetylacetone*, $CH_3\cdot CO\cdot CH_2\cdot CO\cdot CH_3$. They contain two hydrogen atoms replaceable by metals. These atoms must belong to the methylene-group between two negative carbonyl-groups, since diketones of the formula $R\cdot CO\cdot (Alk.*)_2\cdot CO\cdot R$ cannot yield metallic derivatives.

Acetylacetone is obtained by the condensation of ethyl acetate and acetone. It is a colourless liquid of agreeable odour, boils at 137°, and at 15° has the density 0·979. Boiling with water decomposes it into acetone and acetic acid, a reaction affording another example of the instability of compounds containing a carbon atom loaded with negative groups.

Among the salts of acetylacetone are the copper salt, $(C_5H_7O_2)_2Cu$, sparingly soluble in water; and the volatile aluminium salt, $(C_5H_7O_2)_3Al$. By a determination of the vapour-density of this compound, Combes proved the aluminium atom to be tervalent.

These metallic compounds have properties differing from those of ordinary salts. Unlike true salts, they are soluble in benzene, chloroform, and other organic solvents. Their aqueous solutions are almost non-conductors of electricity. They either do not answer the ordinary tests

* *Alk.* = methyl or its homologues.

for the metals, or else react very slowly. The ferric and aluminium salts are of very weak basicity and acidity, and do not undergo hydrolytic dissociation but diffuse unchanged through parchment-paper. In these respects they resemble mercuric cyanide ("Inorganic Chemistry," **283**), a substance practically not ionized in aqueous solution, and therefore lacking all the properties characteristic of ordinary salts.

A type of the 1:4-*diketones* is *hexane*-2:5-*dione* or *acetonylacetone*,

$$CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO \cdot CH_3,$$

prepared as described in **233**, 4. It is a colourless liquid of agreeable odour, boils at 193°, and at 21° has the density 0·970. Acetonylacetone and other 1:4-diketones yield cyclic compounds, considered in **392–396**.

Halogen-substituted Aldehydes.

201. *Chloral* or trichloroacetaldehyde, $CCl_3 \cdot C\langle^{H}_{O}$, is of great therapeutic importance, since with one molecule of water it forms a crystalline compound termed *chloral hydrate*, and employed as a soporific. Chloral is prepared technically by saturating ethanol with chlorine. The alcohol must be as free from water as possible, and the chlorine dried carefully. At first the reaction-mixture is cooled artificially, but after a few days the process becomes less energetic, and the temperature is raised slowly to 60°, and finally to 100°.

The initial product of the action of chlorine on ethanol is *ethyl hypochlorite*:

$$CH_3 \cdot CH_2 \cdot OH + Cl_2 = CH_3 \cdot CH_2 \cdot OCl + HCl.$$

This compound quickly loses hydrogen chloride to form *ethanal*, and it changes to *chloroethanal*:

$$CH_3 \cdot CH_2 \cdot OCl = CH_3 \cdot CHO + HCl;$$
$$CH_3 \cdot CHO + Cl_2 = CH_2Cl \cdot CHO + HCl.$$

A substance of the formula $CH_2Cl \cdot CH\langle^{OH}_{OC_2H_5}$ is produced by the union of ethanol and chloroethanal, and is then attacked by hydrogen chloride and ethanol to form *dichloroether* by reaction I and *chloroacetal* by reaction II:

I. $$CH_2Cl \cdot CH\langle^{OH}_{OC_2H_5} + HCl = CH_2Cl \cdot CHCl \cdot OC_2H_5 + H_2O;$$

II. $$CH_2Cl \cdot CH\langle^{OH}_{OC_2H_5} + C_2H_5OH = CH_2Cl \cdot CH(OC_2H_5)_2 + H_2O.$$

Chlorine converts dichloroether into *trichloroether*, $CHCl_2 \cdot CHCl \cdot OC_2H_5$, the same compound being formed from chloroacetal by hydrogen chloride and chlorine:

$$CH_2Cl\cdot CH(OC_2H_5)_2+HCl+Cl_2=$$
$$=CHCl_2\cdot CHCl\cdot OC_2H_5+C_2H_5OH+HCl.$$

The water produced in the process transforms the trichloroether into *dichloroacetaldehyde alcoholate*:

$$CHCl_2\cdot CHCl(OC_2H_5)+H_2O=CHCl_2\cdot CH<\begin{matrix}OH\\OC_2H_5\end{matrix}+HCl.$$

At a higher temperature this alcoholate undergoes slow chlorination to *chloral alcoholate:*

$$CHCl_2\cdot CH<\begin{matrix}OH\\OC_2H_5\end{matrix}+Cl_2=CCl_3\cdot CH<\begin{matrix}CH\\OC_2H_5\end{matrix}+HCl.$$

This substance is the final product of chlorination, and chloral is obtained from it by the action of concentrated sulphuric acid.

Chloral is an oily liquid of penetrating odour, boils at 97°, and at 20° has the density 1·512. Water converts it with evolution of heat into the well-crystallized chloral hydrate, melting at 57°. To this compound is assigned the formula $CCl_3\cdot CH<\begin{matrix}OH\\OH\end{matrix}$, as it does not possess all the aldehyde-reactions. This lack is exemplified by its inability to restore the red tint of a solution of magenta (**373**) decolorized by sulphurous acid (**107**, 3), and marks chloral hydrate as one of the few compounds containing two hydroxyl-groups in union with a single carbon atom (**127, 149, 204, 230, 234**).

In other respects chloral behaves as an aldehyde, reducing an ammoniacal silver solution with formation of a mirror, combining with sodium hydrogen sulphite, and undergoing oxidation by nitric acid to trichloroacetic acid. Solutions of the alkalis decompose it at the ordinary temperature with production of chloroform and formic acid:

$$\begin{matrix}CCl_3\cdot\\+\ H\end{matrix}\Big|\begin{matrix}C\overset{H}{\underset{HO}{O}}\end{matrix}=CCl_3H+HC\begin{matrix}O\\\diagdown\\OH\end{matrix}.$$

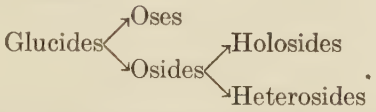
On account of its purity, chloroform prepared in this manner is preferred for anæsthetization.

In dilute solutions of about centinormal strength, and at low temperature, this reaction has a measurable velocity. Experiment has proved it to be unimolecular, and not bimolecular as indicated by the equation. This phenomenon is explicable by assuming preliminary combination of the base and chloral hydrate to form a salt of the type $CCl_3\cdot CH<\begin{matrix}OH\\OK'\end{matrix}$ subsequently decomposed into chloroform and formate. The electric conductivity of a mixture of solutions of chloral hydrate and a base also indicates a union of the molecules.

ALDEHYDO-ALCOHOLS AND KETO-ALCOHOLS OR CARBOHYDRATES.

202. The sugars, starch, and cellulose occupy a prominent place among natural products. As most of them have the composition $C_n(H_2O)_m$, they are termed *carbohydrates*, a name indicating the presence of carbon in union with the elements of water. They are also entitled *glucides*.

The carbohydrates are classified in two main groups. One of these groups comprises those not transformable into simpler substances, yet possessing all the carbohydrate characteristics. Its members are termed *oses*. The second group includes carbohydrates convertible by hydrolysis into oses only, or into oses and compounds of varied nature. The individuals of this class are named *osides*, the first type being entitled *holosides*, and the second *heterosides*. This classification corresponds with the scheme



The oses are also termed *monosaccharides* or *monoses*, and the holosides *polysaccharides* or *polyoses*.

Nomenclature and General Properties of the Monoses and their Derivatives.

When the monoses are aldehydes they are designated *aldoses*, and when ketones, *ketoses*. The number of carbon atoms in the molecule is indicated by their names, such as *pentose*, *hexose*, *heptose*, etc. To distinguish between aldoses and ketoses the prefixes " aldo- " and " keto-" are employed; as *aldohexose*, *ketohexose*, and so on.

Polyoses capable of being regarded as derived from two monose molecules by the elimination of one molecule of water are termed *dioses*, those formed from two molecules of hexose being named *hexodioses*. The polyoses derived from three monose molecules by the elimination of two molecules of water are called *trioses*, as *hexotriose*, etc.

The aldoses are converted by oxidation into monobasic acids containing the same number of carbon atoms, the pentoses yielding the monobasic *pentonic acids*, the hexoses the *hexonic acids*, and so on. The oxidation can be carried further to yield a dibasic acid containing the same number of carbon atoms as the parent aldose. Oxidation converts the ketoses into acids with a smaller number of carbon atoms.

On reduction, the aldoses and ketoses take up two hydrogen atoms, with formation of the corresponding alcohols, hexose yielding a *hexahydric alcohol*, and pentose a *pentahydric alcohol* (204 and 207).

203. Four reactions characteristic of all monoses are known:

1. Under the influence of heat they reduce an ammoniacal silver solution, forming a metallic mirror.

2. When warmed with alkalis, they give a yellow coloration turning brown, and ultimately resinify.

3. On heating an alkaline copper solution (Fehling or Ost, 191) with a solution of a monose, the yellow-red suboxide of copper is formed by reduction.

> Trommer's test involves dissolving the monose in a solution of sodium hydroxide, and adding a few drops of a solution of cupric sulphate. Heating precipitates cuprous oxide from the blue liquid obtained.

4. When a monose is heated with excess of phenylhydrazine, $C_6H_5 \cdot NH \cdot NH_2$, in dilute sulphurous-acid solution, a yellow compound crystallizing in fine needles is produced. Substances of this type are insoluble in water, and are termed *osazones*. Their formation admits of the following explanation.

In some reactions the behaviour of the sugars accords with the presence of the group —CHOH—CO—. The action of phenylhydrazine (310) on a carbonyl-group has been explained already (103), water being eliminated and a hydrazone formed:

$$\begin{array}{l} | \\ C\boxed{O+H_2}N \cdot NHC_6H_5 = C : N \cdot NHC_6H_5 + H_2O. \\ | \end{array}$$

A second molecule of phenylhydrazine then reacts with the group —CHOH—, expelling two hydrogen atoms, the molecule of phenylhydrazine being decomposed into ammonia and aniline (297):

$$\underset{\text{Phenylhydrazine}}{C_6H_5 \cdot NH \cdot NH_2} = \underset{\text{Aniline}}{C_6H_5 \cdot NH_2} + NH_3.$$
$$+ \quad H\ H$$

The elimination of two hydrogen atoms from the group —CHOH— converts it into a carbonyl-group, —CO—, and with it a third molecule of phenylhydrazine reacts to form a hydrazone, the group

$$\begin{array}{l} | \\ CHOH \\ | \\ CO \\ | \end{array} \text{ being converted into } \begin{array}{l} | \\ C{=}N \cdot NHC_6H_5 \\ | \\ C{=}N \cdot NHC_6H_5 \\ | \end{array}.$$

This group is characteristic of the osazones.

In this reaction the best solvent for the phenylhydrazine is aqueous sulphurous acid, atmospheric oxidation of the base being retarded greatly by the presence of this acid. The procedure is to heat a mixture of the reagent and an aqueous solution of the sugar on a water-bath, the osazone being precipitated in a very pure condition.

The osazones dissolve in water with difficulty, a property of service in the separation of the monoses. These sugars are very soluble in water, crystallize with great difficulty especially in presence of salts, and often cannot be purified by crystallization. By means of the sparingly soluble osazones they can be separated, the osazones being obtained readily in the pure state by crystallization from a dilute solution of pyridine (387). A determination of the melting-point of the osazone obtained from it furnishes a method of identifying a monose.

Constitution of the Monoses.

204. As is demonstrated in the sequel, the constitution of all the monoses follows from that of the aldohexoses, whose structure is derived from the following considerations:

1. The aldohexoses have the molecular formula $C_6H_{12}O_6$.

2. Almost all the known hexoses contain a normal chain of six carbon atoms, since they can be reduced to a hexitol converted by further reduction with hydrogen iodide at a high temperature into 3-iodohexane, $CH_3 \cdot CH_2 \cdot CHI \cdot CH_2 \cdot CH_2 \cdot CH_3$.

The constitution of this iodide is inferred from its conversion into an alcohol transformed by oxidation into $CH_3 \cdot CH_2 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CH_3$, since further oxidation of this product yields *n*-butyric acid and acetic acid.

3. In presence of hydrochloric acid as a catalyst, hexoses combine with boiling methyl alcohol and other alcohols, the reaction being attended by the elimination of water. As in many respects the products are analogous to the natural glucosides or heterosides (206), they are termed *glucosides*.

The formation of *methylglucoside* is typical, and can be represented by the equation

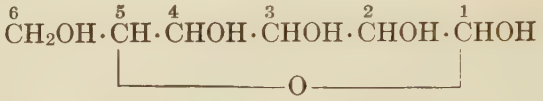
$$C_6H_{12}O_6 + CH_3OH = C_6H_{11}O_6 \cdot CH_3 + H_2O.$$

One hydrogen atom of the hexose becomes replaced by a methyl-group. Since hydrolysis eliminates this group readily, its union in the hexose must be through oxygen, indicating the presence in the hexose of at least one hydroxyl-group.

The hexoses contain four additional hydroxyl-groups, as can be proved by converting them into penta-acetyl-derivatives through heating with acetic anhydride and a small proportion of sodium acetate or

of zinc chloride. Methylation of methylglucoside by dry silver oxide and methyl iodide substitutes methyl-groups for four additional hydrogen atoms, these groups being removable by hydrolysis, although not so readily as the methyl-group of the parent methylglucoside. This reaction indicates the hexose hydroxyl-group concerned in the formation of the glucoside to occupy a special position in the molecule.

As normally an individual carbon atom is not in union with two or three hydroxyl-groups, the facts cited find expression in the structural formula



The hydroxyl-group at carbon atom 1 occupies a special position, and the formula expresses the mechanism of the formation of methylglucoside. In this compound the hydrogen atom of hydroxyl-group 1 of the hexose becomes replaced by a methyl-group. This formula accords also with the other properties of the hexoses:

(*a*) Reduction to the sexavalent alcohol through addition of two hydrogen atoms. One of these atoms unites with carbon atom 1 to give the group CH_2OH; the other becomes attached to the "ether" oxygen atom (┘—O—└), producing a hydroxyl-group at carbon atom 5.

(*b*) Oxidation to a monobasic acid with the same number of carbon atoms. In practice this oxidation yields the corresponding lactone (**185**), the two hydrogen atoms at carbon atom 1 being removed.

(*c*) Further oxidation to a dibasic acid with the same number of carbon atoms, the primary CH_2OH-group 6 being capable of undergoing transformation into a carboxyl-group.

(*d*) The power possessed by the hexoses of reacting in some respects like the aldehydes (**203**, 1 and 2). Addition to a hexose of one molecule of water changes the formula to

The group $CH(OH)_2$ is known to behave in many reactions as an aldehydo-group, $-C\overset{H}{\underset{O}{}}$ (**201**), and its formation explains the production of osazones.

The lack of an aldehydo-group at carbon atom 1 accords with the failure of the hexoses to display *all* the reactions characteristic of aldehydes. They do not combine with sodium hydrogen sulphite, nor

polymerize readily, and they are unable to restore the colour to SCHIFF'S reagent (107, 3).

In the sequel the group $\begin{matrix}-CHOH\\ |\\ -O\end{matrix}$ at 1 will often be termed the "Active group."

205. The formula given for the hexoses involves two rather arbitrary assumptions, one as to the ether oxygen atom being attached to carbon atoms 1 and 5, and the other respecting the relative distribution of the hydroxyl-groups and the carbon atoms. The first assumption accords with the structure of most lactones (185), but its accuracy admits of more complete demonstration (207). The fact of the existence of certain monoses with a different mode of linking for this oxygen atom will be considered later.

The second assumption agrees with the principle (149) of a carbon atom usually being unable to unite with more than one hydroxyl-group. A more convincing proof of the absence from the monoses of two hydroxyl-groups attached to the same carbon atom is afforded by the following considerations.

Reduction of a hexose, $C_6H_{12}O_6$, to a hexahydric alcohol, $C_6H_{14}O_6$, involves the addition of two hydrogen atoms only, and this addition must occur in the manner indicated, since the carbon chain remains unbroken. If the hexose contain two hydroxyl-groups attached to one carbon atom, there must be a similar arrangement in the hexahydric alcohol derived from it. Compounds containing a carbon atom in union with two hydroxyl-groups lose water readily with formation of aldehydes or ketones, and they possess most of the properties characteristic of these substances (201). In contrast, the hexahydric alcohols have an exclusively alcoholic character, and do not exhibit any of the reactions of aldehydes and ketones. Consequently, neither the hexahydric alcohols nor the hexoses can contain two hydroxyl-groups attached to a single carbon atom.

The possibility of the union of three hydroxyl-groups with one carbon atom is excluded also, the production of a compound with such a grouping always being prevented by the elimination of water to form an acid (79):

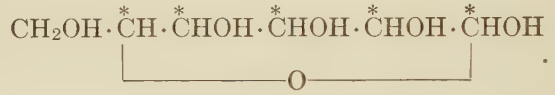
$$\begin{matrix}OH\\ |\\ -CO-H.\\ |\\ OH\end{matrix}$$

The monoses have not any of the properties characteristic of acids; their aqueous solutions do not conduct the electric current, although

the dissociation-constant of an acid containing so many hydroxyl-groups should be considerably higher than that of a saturated fatty acid such as acetic acid (180).

With calcium and strontium hydroxides and other bases the carbohydrates form compounds termed *saccharates*, and belonging to the class of alkoxides (50).

These considerations demonstrate the constitution of the aldohexoses to be that indicated, and the same method of proof being applicable to each member, all of them must have the same constitutional formula and be stereoisomerides. This similarity is due to the presence in the molecule of asymmetric carbon atoms, an aldohexose having five such atoms indicated by asterisks in the formula

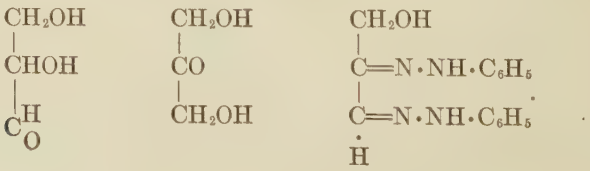


Methods of Formation of the Monoses.

206. 1. The monoses are produced from the polyoses by hydrolysis, the transformation being attended by the addition of the elements of water. They are formed also by the hydrolysis of *heterosides* or *glucosides*. These substances are natural products, decomposed by enzymes or by dilute acids into a carbohydrate, and one or more other compounds often of very divergent character. An example is *amygdaloside* or *amygdalin* (256).

2. The monoses are derived also from the corresponding alcohols by the action of oxidizers such as nitric acid. Arabitol, $C_5H_{12}O_5$, yields arabinose, $C_5H_{10}O_5$; xylitol yields xylose; mannitol yields mannose; etc.

Careful oxidation of glycerol with hydrogen peroxide in presence of ferrous salts, or with bromine and sodium carbonate, produces a viscous liquid termed glycerose with the four reactions typical of monoses (203). Prepared by the first method, it is essentially glyceraldehyde (I); by the second method, only dihydroxyacetone (II) is produced. Both compounds yield the same osazone, *glycerosazone* (III), a substance crystallizing in yellow leaflets and melting at 131°:



In accordance with the nomenclature indicated, glycerose is a *triose*.

When sorbose-bacteria are cultivated in a solution of glycerol, the final product of the action of the atmospheric oxygen is dihydroxyacetone. These bacteria can oxidize to ketoses other polyhydric alcohols also.

3. Another method of formation depends on replacement by hydroxyl of the bromine in bromo-derivatives of aldehydes, effected by the action of cold baryta-water.

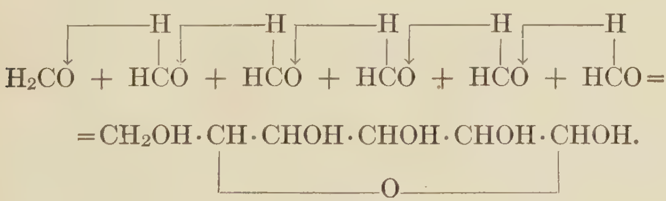
In this manner the simplest member of the sugars, *glycolose* or *glycollaldehyde*, $CH_2OH\cdot C^{H}_{O}$, is obtained from monobromoaldehyde, $CH_2Br\cdot C^{H}_{O}$. Glycolose displays all the reactions of the monoses, crystallizes well, and melts about 97° with decomposition. It polymerizes readily, and is volatile with steam.

The addition of bromine to acraldehyde (141) yields

$$CH_2Br\cdot CHBr\cdot C^{H}_{O},$$

convertible by the action of barium-hydroxide solution into glyceraldehyde.

4. Monoses are derived also from formaldehyde by the action of lime-water (aldol-condensation). The crude condensation-product, termed *formose*, is a sweet viscous substance, and consists of a mixture of compounds of the formula $C_6H_{12}O_6$. In this reaction six molecules of formaldehyde undergo the aldol-condensation (106):



A hexose can be obtained also from glyceraldehyde, two molecules of it yielding by the aldol-condensation one molecule of the hexose. This hexose is named *acrose* from its relationship to acraldehyde, a substance producing glyceraldehyde by method 3. Acrose is a constituent of formose, and displays the optical inactivity characteristic of all compounds prepared by purely chemical synthesis.

5. Monoses can be transformed into other monoses with one carbon atom more or less in the molecule by the aid of step-by-step synthetical or analytical methods, as indicated in the subjoined examples. Monoses can form an addition-product with hydrogen cyanide. An aldohexose

yields a cyanohydrin convertible by hydrolysis into a monobasic acid containing seven carbon atoms,

$$\overset{7}{C}H_2OH\cdot\overset{6}{C}HOH\cdot\overset{5}{C}HOH\cdot\overset{4}{C}HOH\cdot\overset{3}{C}HOH\cdot\overset{2}{C}HOH\cdot\overset{1}{C}OOH.$$

The 4-hydroxyl-group reacts easily with the carboxyl-group to form a lactone,

$$CH_2OH\cdot CHOH\cdot CHOH\cdot \underbrace{CH\cdot CHOH\cdot CHOH\cdot CO}_{O}.$$

In aqueous solution, these lactones can be reduced by sodium-amalgam to the corresponding aldehydes, the aldoses.

By repeated application of the cyanohydrin-synthesis, and reduction of the lactone obtained, it has been possible to prepare *decoses*, with ten carbon atoms.

The step-by-step decomposition of monoses can be effected by other agencies, an example being the conversion of pentoses into tetroses. The calcium salts of the pentonic acids, obtained from these pentoses by oxidation, can be oxidized further by hydrogen peroxide in presence of ferric acetate:

$$\underset{\text{Pentonic acid}}{CH_2OH\cdot(CHOH)_3\cdot COOH}+O=\underset{\text{Tetrose}}{CH_2OH\cdot(CHOH)_2\cdot C{}^{H}_{O}}+CO_2+H_2O.$$

Another process consists in the application of Hoogewerff and van Dorp's method (**259**) with sodium hypochlorite to the amides formed from monobasic acids, such as gluconic acid:

$$\underset{\text{Gluconamide}}{CH_2OH\cdot(CHOH)_4\cdot CONH_2}\xrightarrow{NaOCl}CH_2OH\cdot(CHOH)_4\cdot NCO\rightarrow$$

$$\xrightarrow{NaOH}\underset{\text{Arabinose}}{CH_2OH\cdot(CHOH)_3\cdot C{}^{H}_{O}}+NaNCO.$$

Among the *natural products* of this type the hexoses and their polyoses constitute by far the greatest proportion, the pentoses also occurring abundantly as polyoses. Natural heptoses are very scarce, and the trioses, tetroses, and higher monoses can be obtained only synthetically.

I. MONOSES.

Pentoses.

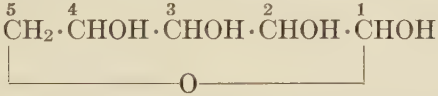
207. Certain different pentoses have been identified, among them *arabinose* and *xylose*, both present in many plants as polyoses termed *pentosans*.

Arabinose can be prepared by boiling gum-arabic or cherry-gum with dilute acids, but the best method is to hydrolyze sliced sugar-beet after extraction of the sugar, the resulting mixture of galactose and arabinose being freed from galactose by fermentation. A yield of eight to twelve per cent. can be produced from the husks of cotton-seed.

Xylose, or *wood-sugar*, can be obtained similarly from bran, wood, straw, and other substances, especially the shells of apricot-stones. Arabinose and xylose can be prepared from any plant-cells converted into wood, and displaying the reaction of lignin (**228**). The racemic modification of arabinose is present in the urine of patients suffering from the disease known as *pentosuria*.

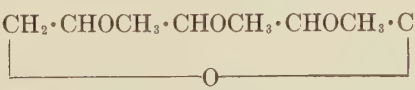
Arabinose forms well-defined crystals, melts at 160°, and has a sweet taste. Its osazone melts at 157°. Xylose also crystallizes well, and yields an osazone melting at 160°.

Arabinose and xylose are aldoses and have the same formula,



This constitution is indicated by their conversion through gentle oxidation with bromine-water into *arabonic acid* and *xylonic acid* respectively. Since each of these acids has the formula $CH_2OH \cdot (CHOH)_3 \cdot COOH$, they are stereoisomeric. On stronger oxidation, both arabinose and xylose yield *trihydroxyglutaric acid*, $COOH \cdot (CHOH)_3 \cdot COOH$, its constitution following from its reduction to glutaric acid. The acid obtained from arabinose is optically active, and that from xylose is inactive, indicating them to be stereoisomerides.

By methylating xylose Hirst and Purves demonstrated the ether oxygen atom of that pentose to be in union with carbon atoms 1 and 5. The product is a tetramethyl-derivative, indicated to have the structure



by its oxidation to trimethoxyglutaric acid,

$$HOOC \cdot CHOCH_3 \cdot CHOCH_3 \cdot CHOCH_3 \cdot COOH.$$

Obviously this acid could not be obtained from a substance with its ether oxygen atom in union with other carbon atoms of the chain.

This method of methylation followed by oxidation is applicable also to identifying the position of the ether oxygen atom in any of the other monoses. The first operation exchanges the free hydroxyl-groups of the sugar molecule for the more stable methoxyl-groups, thereby preventing any change in the position of the oxygen-bridge during the subsequent oxidation (**220**).

On reduction, arabinose yields *arabitol* and xylose gives *xylitol*, these pentahydric alcohols being stereoisomeric. Arabinose and xylose can be converted into hexoses by the cyanohydrin-synthesis, a proof of their lack of a carbon atom in union with more than one hydroxyl-group (**205**), and of their possession of a normal carbon chain:

$$\underbrace{\overbrace{CH_2\cdot(CHOH)_3\cdot CHOH}^{}}_{\text{—O—}} \rightarrow CH_2OH\cdot(CHOH)_3\cdot CH{<}^{OH}_{CN} \rightarrow$$

Pentose

$$\rightarrow CH_2OH\cdot(CHOH)_3\cdot CHOH\cdot COOH.$$

Hexonic acid

This hexonic acid yields a lactone convertible by reduction into the hexose. Arabinose and xylose contain four asymmetric carbon atoms, and are optically active.

Apiose is considered in **213**.

The pentoses cannot be fermented. They have one common property serving for their recognition and distinction from hexoses. Boiling with dilute sulphuric acid, or with hydrochloric acid of density 1·06, converts the pentoses and their polyoses into the volatile *furfural*, $C_5H_4O_2$ (**393**). With aniline and hydrochloric acid it yields an intense red dyestuff.

The presence of the polyose of xylose can be detected in such a substance as straw by distillation with hydrochloric acid of density 1·06. With aniline and hydrochloric acid the distillate gives an intense red coloration, and with phenylhydrazine yields a phenylhydrazone very sparingly soluble in water. Each of these reactions indicates the presence of furfural.

Hexoses.

208. The *hexoses* are colourless compounds of sweet taste, are difficult to crystallize, and incapable of being distilled without decomposition. They dissolve readily in water, with difficulty in absolute alcohol, and are insoluble in ether. Since all the aldohexoses are stereoisomerides (**205**), their oxidation-products, the monobasic and dibasic acids, are stereoisomerides also.

1. *Dextrose* (d-*glucose* or *grape-sugar*), $C_6H_{12}O_6,H_2O$, is the hexose present in much the largest proportion in fruits of sweet taste, ripe grapes containing 20 to 30 per cent. It is found in the urine of diabetic patients, and in small proportion in normal urine. It can be obtained from many polyoses, the process being exemplified by the hydrolytic *inversion* (**216**) of sucrose to a mixture of dextrose and lævulose (**209**) termed *invert-sugar*. The technical preparation of dextrose from starch by boiling with dilute acids likewise depends on hydrolysis.

Dextrose crystallizes from water or alcohol with difficulty. Acetic acid is the most suitable solvent, the crystals obtained from it lacking water of crystallization, and melting at 146°. In **43** mention is made of the aptitude of dextrose for fermentation, the chief products being alcohol and carbon dioxide. Natural dextrose is dextrorotatory: a lævorotatory and an optically inactive modification have been prepared artifically. The dextrorotatory, lævorotatory, and optically inactive isomerides are distinguished by the prefixes *d* (*dexter*), *l* (*lævus*), and *i* (*inactive*); thus, *d*-glucose, *l*-glucose, *i*-glucose.

By convention, all other monoses derived from a *d*-hexose, *l*-hexose, or *i*-hexose also are distinguished by the letters *d*, *l*, or *i*, even if possessing a rotatory power opposite in sign to that indicated by these letters. Thus, lævulose or ordinary fructose can be obtained from dextrose or *d*-glucose, and is lævorotatory, but also is named *d*-fructose on account of its genetic relationship to *d*-glucose. The same method of classification is adopted for the hexahydric alcohols, the hexonic acids, and in general for all derivatives of the hexoses.

Dextrose is an aldose, as is proved by its oxidation to a hexonic acid, d-*gluconic acid*, $CH_2OH\cdot(CHOH)_4\cdot COOH$. Further oxidation produces the dibasic *d*-saccharic acid, $COOH\cdot(CHOH)_4\cdot COOH$.

Saccharic acid gives a characteristic potassium hydrogen salt of slight solubility, its formation serving as a test for dextrose. The substance suspected of containing dextrose is oxidized with nitric acid, any of the hexose present becoming transformed into saccharic acid, and the product being precipitated as potassium hydrogen salt by addition of a concentrated solution of potassium acetate.

On reduction, dextrose yields a hexahydric alcohol, d-*sorbitol*. It gives also an osazone, d-*glucosazone*, soluble with difficulty in water, and crystallizing in yellow needles melting at 205°.

Solutions of dextrose and many other sugars furnish examples of a phenomenon termed *mutarotation*, and discovered by Dubrunfaut. Immediately after solution, such substances have a rotatory power other than that possessed by them after the lapse of a comparatively short

interval of time. Initially an aqueous solution of dextrose produces a rotation $[\alpha]_D = 109{\cdot}6°$, but after some hours it causes a constant rotation $[\alpha]_D = 52{\cdot}5°$. The attainment of a constant rotatory power is hastened greatly by boiling the solution, and is effected instantly by addition of a small quantity of potassium hydroxide or ammonia.

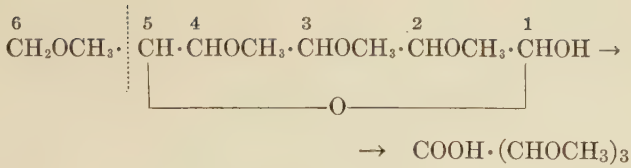
The explanation of this phenomenon must be sought in the partial conversion of the dextrose or other sugar into another modification of different rotatory power. When the rotation has become constant, there is equilibrium between the two modifications.

Tanret prepared three different crystalline modifications of dextrose, denoted by α, β, and γ. α-Dextrose is obtained by crystallization at ordinary temperature from aqueous solvents or from water. It contains one molecule of water of crystallization, and has a specific rotation of $+109{\cdot}6°$. When a concentrated solution of α-dextrose is evaporated at 110°, the residue dissolved in an equal weight of cold water, and absolute alcohol added to the solution, β-dextrose crystallizes. In aqueous solution it has a specific rotation of $+19{\cdot}8°$. When dissolved in water, both these modifications are converted into γ-dextrose, the transformation being slow at ordinary temperatures, but rapid when the solution is boiled or a trace of alkali is added. The γ-form has a specific rotation of $+52{\cdot}50°$. When dissolved in water, it instantly causes this rotation, indicating it not to be an independent form, but a mixture in equilibrium of the α-modification and the β-modification.

By experiment Tanret proved this surmise to be correct. A very concentrated solution of the γ-modification was made, and crystallized at 0°. When a solution of the crystals obtained was prepared at a low temperature, its rotation was diminished by addition of a small quantity of ammonia, proving the crystals to belong to the α-modification. If the γ-form be a mixture of the α-modification and the β-modification, the β-variety must have remained in solution in the mother-liquor, and addition of alkali should increase the rotation of this residual solution. Experiment proved alkali to have this effect.

The stereoisomerism of α-dextrose and β-dextrose is due to the asymmetric carbon atom 1. The two stereoisomeric forms correspond with those of methylglucoside, for with the enzyme maltase α-methylglucoside yields α-dextrose, and with emulsin β-methylglucoside gives β-dextrose. Carbon atom 1 is demonstrated to be the dominant factor by the oxidation of both dextroses to the same gluconic acid.

The epoxy-oxygen atom in dextrose also is united with carbon atoms 1 and 5, as in the formula of **205**. The proof depends on the methylation of dextrose to a tetramethyl-compound convertible by oxidation with nitric acid into a trimethoxypropanedicarboxylic acid, a reaction possible with the 1:5-structure only. This oxidation severs the carbon chain between carbon atoms 5 and 6:



With a small proportion of water, dextrose yields a colourless syrup employed in the preparation of liqueurs and of confectionery.

209. *Lævulose* (d-*fructose* or *fruit-sugar*) accompanies dextrose in most sweet fruits. It is a constituent of invert-sugar (**216**), and of honey, which is chiefly a natural invert-sugar. Hydrolysis of *inulin*, a polyose contained in dahlia-tubers, yields only lævulose, just as that of starch gives dextrose. Lævulose crystallizes with difficulty, being soluble readily in water, although less readily than dextrose. It is fermentable, and at the ordinary temperature it is lævorotatory.

Lævulose is a type of the ketoses, only a few of them being known. Its formula, $CH_2 \cdot CHOH \cdot CHOH \cdot CHOH \cdot COH \cdot CH_2OH$ (with O bridging), is inferred from the following considerations. First, oxidation with mercuric oxide in presence of barium-hydroxide solution, converts it into glycollic acid,

$$CH_2OH \cdot COOH,$$

and trihydroxyglutaric acid,

$$COOH \cdot (CHOH)_3 \cdot COOH.$$

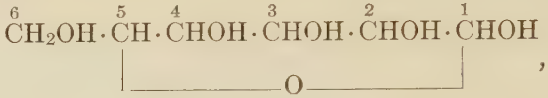
Since the oxidation is at the C(OH)-group, the production of these acids necessitates the adoption of this constitutional formula. Second, application of the cyanohydrin-synthesis to a compound of this constitution would yield a heptonic acid with the formula

$$CH_2OH \cdot (CHOH)_3 \cdot C(OH)(COOH) \cdot CH_2OH.$$

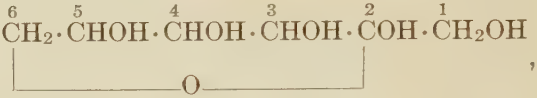
The heptonic acid obtained from lævulose has this constitution, as is proved by heating it at a high temperature with hydrogen iodide, all the hydroxyl-groups being replaced by hydrogen and a heptylic acid being formed. This acid is identical with the synthetic *methyl*-n-*butylacetic acid* (**233**, 2),

$$CH_3 \cdot (CH_2)_3 \cdot CH(COOH) \cdot CH_3.$$

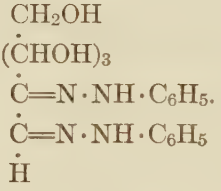
The osazone of lævulose is identical with that of dextrose. A comparison of the formula of dextrose,



with that of lævulose,

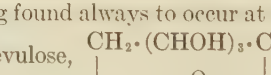


indicates identity of the two osazones to be contingent on the formation of the hydrazone being followed by the union of the 2-carbon atom of dextrose, and the 1-carbon atom of lævulose, with the second phenylhydrazine-residue. In each instance the reaction is located at a carbon atom attached directly to the appropriate characteristic group 1 or 2. For this reason the formation of an osazone is assumed always to involve the union of two phenylhydrazine-residues with neighbouring carbon atoms. d-*Glucosazone*, or d-*fructosazone*, therefore has the constitution



Methylphenylhydrazine, $\begin{matrix}CH_3\\C_6H_5\end{matrix}>N\cdot NH_2$, yields osazones with ketoses only, but converts aldoses into colourless hydrazones separated readily from the intensely yellow osazones. This reagent is a valuable aid in the detection of ketoses.

Careful warming of osazones with hydrochloric acid eliminates two molecules of phenylhydrazine, with formation of *osones*, compounds containing two carbonyl-groups. In this manner *d*-phenylglucosazone yields d-*phenylglucosone*, $CH_2OH\cdot(CHOH)_3\cdot CO\cdot C\overset{H}{\underset{O}{}}$.

The osones can be reduced by zinc-dust and acetic acid, addition of hydrogen being found always to occur at the terminal carbon atom. *d*-Glucosone yields lævulose,  .

The reaction affords a means of converting aldoses into ketoses:

Aldose → Osazone → Osone → Ketose.

Inversely, an aldose can be obtained from a ketose. Reduction of a ketose yields a hexahydric alcohol, converted by oxidation into a monobasic hexonic acid. This substance loses water to form the corresponding lactone, a substance reducible to the aldose:

Ketose → Hexahydric Alcohol → Hexonic Acid → Lactone → Aldose.

210. d-*Mannose* is an aldose, and is present as a polyose in the vegetable-ivory nut. It is obtained also by the careful oxidation of the hexahydric alcohol *mannitol*, found in several plants. *d*-Mannose is a hard, amorphous, hygroscopic substance; it can be fermented readily, and is very soluble in water. It yields a characteristic hydrazone melting between 195° and 200°, and differing from the hydrazones of the other monoses in dissolving in water with difficulty. Oxidation converts *d*-mannose first into the monobasic d-*mannonic acid*,

$$CH_2OH \cdot (CHOH)_4 \cdot COOH,$$

and then into the dibasic d-*mannosaccharic acid*,

$$COOH \cdot (CHOH)_4 \cdot COOH.$$

It yields dextrose by a method generally applicable to the transformation of aldoses into their stereoisomerides. For this purpose it is converted first into *d*-mannonic acid. In a boiling solution in quinoline (**400**) this substance is transformed partly into the stereoisomeric *d*-gluconic acid, its lactone being reducible to dextrose. Inversely, *d*-gluconic acid is changed partly into *d*-mannonic acid by boiling its quinoline solution, dextrose being convertible into *d*-mannose by this procedure.

The stereoisomerism of *d*-mannose and dextrose, as well as that of *d*-mannonic acid and *d*-gluconic acid, is occasioned only by different grouping round the 2-carbon atom, for the osazone of *d*-mannose is identical with that of dextrose:

$$CH_2OH \cdot CHOH \cdot CHOH \cdot CHOH \cdot \overset{2}{C}(=N \cdot NH \cdot C_6H_5) - C(H) = N \cdot NH \cdot C_6H_5 .$$

Identity of these osazones is contingent on that of the residue

$$CH_2OH \cdot (CHOH)_2 \cdot CHOH—$$

in *d*-mannose and dextrose, and the stereoisomerism of these substances can be due only to a difference in the arrangement of the groups in union with the 2-carbon atom.

So far as the transformations of the monobasic hexonic acids effected by boiling with quinoline or pyridine have been studied, the alteration has been found always to occur as in the instance cited at a single carbon atom adjoining the aldehydo-group, the 2-carbon atom.

d-*Galactose* can be obtained by the hydrolysis of lactose, or by the oxidation of the hexahydric alcohol *dulcitol*, a constituent of certain plants. *d*-Galactose is crystalline, melting at 168°; it is strongly dextrorotatory, is capable of undergoing fermentation, and exhibits mutarotation. Galactose is proved to be an aldose by its oxidation to the monobasic d-*galactonic acid*, $C_6H_{12}O_7$. Further oxidation yields the sparingly soluble dibasic *mucic acid*, $COOH \cdot (CHOH)_4 \cdot COOH$, its formation serving to detect *d*-galactose. This test involves oxidizing with nitric acid the hexose under examination. Mucic acid is optically inactive, and cannot be resolved into optically active components.

Their conversion by hydrochloric acid into *lævulic acid* (**234**) constitutes a general reaction for the hexoses. Brown amorphous masses termed *humic substances* are produced at the same time. Lævulic acid can be identified by means of its silver salt, a derivative dissolving with difficulty and yielding characteristic crystals.

The identification of the constituents of a mixture of monoses often can be effected readily by the aid of phenylhydrazine and its substitution-products (**310**), the tendency of each monose to form a phenylhydrazone or osazone depending on the particular hydrazine-derivative employed. From a solution containing arabinose and dextrose unsymmetrical methylphenylhydrazine, $C_6H_5 \cdot N(CH_3) \cdot NH_2$, dissolved in acetic acid precipitates arabinosemethylphenylhydrazone. After filtering to remove the hydrazone and warming the liquid with an acetic-acid solution of phenylhydrazine, phenylglucosazone crystallizes.

The monoses can be recovered readily from their phenylhydrazones by heating these derivatives with benzaldehyde or with formaldehyde, the hydrazone of the aldehyde utilized being formed. In some instances this method furnishes a very good means of obtaining monoses in the pure state.

Synthesis of the Monoses.

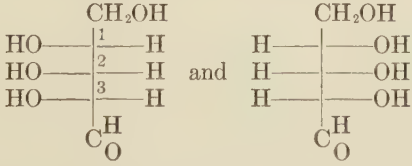
211. As mentioned in **206**, 4, condensation of formaldehyde or of glyceraldehyde yields compounds of the formula $C_6H_{12}O_6$. Similar derivatives are produced by the condensation of glycollaldehyde. These substances are in the form of a syrup or concentrated aqueous solution. A phenylhexosazone identical with the osazone of inactive glucose, fructose, or mannose is obtained from these syrups by the action of phenylhydrazine, such synthetic products always being racemic mix-

tures. Elimination of two phenylhydrazine-residues yields an osone, convertible by reduction into *dl*-fructose (**209**). Further reduction of this monose gives *dl*-mannitol, transformed by oxidation into *dl*-mannose as primary product, and then into *dl*-mannonic acid. Resolution of this acid into its optical components yields *d*-mannonic acid, convertible by reduction into *d*-mannose. This substance can be transformed into dextrose (*d*-glucose) by the method of **210**, and from either monose it is possible to obtain lævulose (*d*-fructose) by the process described in **209**. From these hexoses the preparation of pentoses such as *d*-arabinose and *l*-xylose can be effected by oxidation with hydrogen peroxide of the calcium salt of the hexonic acid in presence of ferric acetate as catalyst. Oxidation of *l*-xylose produces *l*-xylonic acid, a substance converted by boiling with pyridine into the isomeric lyxonic acid, this product being reducible to *d*-lyxose. By means of the cyanohydrin-synthesis this derivative can be transformed into *d*-galactonic acid, a compound reducible to *d*-galactose.

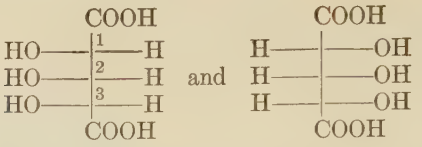
Stereochemistry of the Monoses.

212. As stated in **205**, all the aldohexoses and aldopentoses have the same structure, and in consequence their isomerism is stereoisomerism. Although it would be beyond the scope of this book to derive the configuration of all the pentoses and hexoses mentioned therein, it is desirable to indicate the normal procedure for such compounds with several asymmetric carbon atoms in the molecule. For the sake of clarity the stereochemical formulæ employed in this section represent the aldehydic structure of the monoses, $CH_2OH\cdot(CHOH)_4\cdot C\overset{H}{\underset{O}{}}$, but with the hexose formula induced in **205** the method of proof would be similar.

The presence of two dissimilar asymmetric carbon atoms in a molecule is cited in **188** as causing the existence of a greater number of stereoisomerides than that of two similar asymmetric carbon atoms. A projection-formula indicates the principle to apply to a greater number of asymmetric carbon atoms in the molecule. The projection-formulæ for two aldopentoses,



cannot be made to coincide by rotation in the plane of the paper (**190**), proving the aldopentoses not to be identical. In contrast, the corresponding trihydroxyglutaric acids

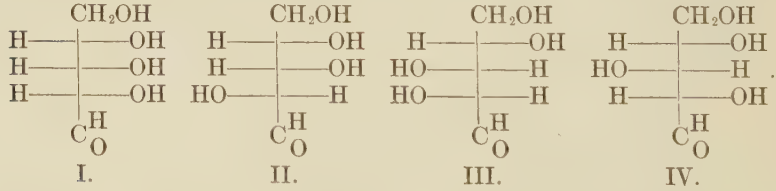


are identical, their projection-formulæ being superimposable. In these compounds the asymmetric carbon atoms 1 and 3 are similar, whilst in the pentoses they are dissimilar.

Assuming the determination of the configuration of a trihydroxyglutaric acid to be possible, and to lead to the projection-formula given, the pentose yielding this acid by oxidation must have one of the foregoing configurations, all others being excluded. It remains only to distinguish between these two configurations.

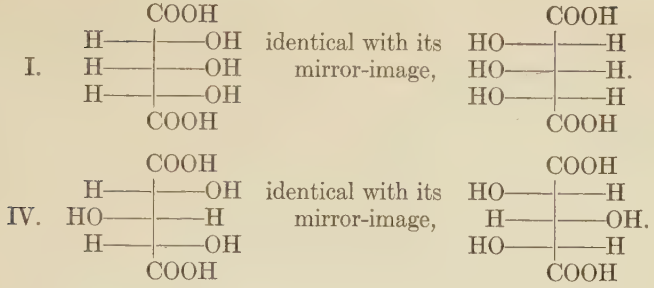
As a prelude to the identification of the stereochemical structure of a pentose, that of the corresponding trihydroxyglutaric acid must be determined. The optical behaviour of these acids affords a means of ascertaining their stereochemical structure. Xylose is optically active, and is converted by oxidation into an optically inactive trihydroxyglutaric acid melting at 152°. Since in this instance an optically inactive substance is obtained from an optically active product and not from a racemic compound, the inactivity must be due to intramolecular compensation, a fact to be expressed in the configuration allotted to this particular trihydroxyglutaric acid. The projection-formula of a compound optically inactive on account of intramolecular compensation must fulfill this condition: it and its mirror-image must be capable of being made to coincide by rotation in the plane of the paper; in other words it and its mirror-image must be identical. Otherwise, the two enantiomorphous configurations of the formula and its mirror-image would be possible, whereas intramolecular compensation admits of only one configuration.

This reasoning can be applied to the determination of the stereochemical structure of arabinose. Eight stereoisomeric formulæ are possible for a pentose, but by arranging them in pairs of mirror-images, and taking one of each pair, four different types are obtained:

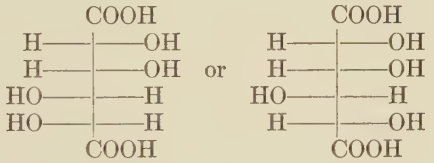


The mirror-image of I is represented on p. 247.

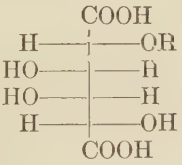
Arabinose is converted by oxidation into an optically active trihydroxyglutaric acid. This fact excludes the trihydroxyglutaric acids obtainable from types I and IV, each of them being superimposable on its mirror-image, and therefore optically inactive:



The fact of the conversion of arabinose by the aid of the cyanohydrin-synthesis into a mixture of dextrose and mannose, transformed by oxidation into the optically active saccharic acid and mannosaccharic acid, enables a choice between types II and III to be made. Since in the cyanohydrin-synthesis only the group $C\overset{H}{\underset{O}{}}$ in $CHOH \cdot C\overset{H}{\underset{O}{}}$ is altered, the configuration of the rest of the carbon atoms remaining unchanged, saccharic acid and mannosaccharic acid must have the stereochemical structure



if arabinose be represented by formula II. As neither of these formulæ can be made to coincide with its mirror-image, formula II is assumed to represent arabinose. Formula III is excluded, as it would involve the stereochemical constitution



for one of the acids mentioned, the substance being identical with its mirror-image. This formula would demand the optical inactivity of one of the acids, and would not accord with the facts.

Arabinose has therefore a formula of the type II, but it is still uncertain whether it should be represented by the formula given or by its mirror-image.

Important aid in the determination of configuration is furnished by the building-up and the breaking-down of the monose molecules. The oxida-

tion of erythrose yields mesotartaric acid, a fact establishing the grouping round the central carbon atoms of this tetrose. Since erythrose is a decomposition-product of *d*-arabinose, this reaction affords a partial insight into the configuration of that pentose. As already indicated, synthesis by the cyanohydrin-method enables the grouping in the hexoses to be inferred from the known configuration of the pentoses.

II. DIOSES.

213. Most of the *dioses* (or *bioses*) known are derived exclusively from hexoses, and therefore have the formula

$$C_{12}H_{22}O_{11} = 2C_6H_{12}O_6 - H_2O.$$

Dioses hydrolyzable to a pentose and a hexose are of very rare occurrence. Hydrolysis of *vicianin*, a glucoside present in the seed of the vetch (*Vicia angustifolia*), yields hydrogen cyanide, benzaldehyde, and a diose *vicianose* proved by its hydrolysis to be formed from dextrose and *l*-arabinose:

$$\underset{\text{Vicianose}}{C_{11}H_{20}O_{10}} + H_2O = \underset{\text{Dextrose}}{C_6H_{12}O_6} + \underset{l\text{-Arabinose}}{C_5H_{10}O_5}$$

Apiin, a glucoside present in parsley, is converted by the action of acids into a diose transformed by further hydrolysis into dextrose and *apiose*, a pentose proved by its oxidation to *iso*valeric acid to have a branched carbon chain.

The hydrolysis can be effected not only by boiling with dilute acids but also by the action of enzymes (**222**). On account of their ready decomposition by water, the monoses constituting a diose are not assumed to be united through the carbon atoms, but through one or more oxygen atoms.

Maltose.

214. In the crystallized state *maltose* has the formula

$$C_{12}H_{22}O_{11},H_2O.$$

It can be prepared from starch by the action of diastase (**43**), and is an important intermediate product in the industrial production of alcohol.

Maltose crystallizes in small white needles, and is strongly dextrorotatory. Boiling it with dilute mineral acids yields dextrose only. It exhibits all the characteristics of the monoses: thus, it reduces an alkaline copper solution; yields an osazone, *maltosazone*,

$$(C_{12}H_{22}O_{11} - 2H_2O - 2H + 2C_6H_5NH \cdot NH_2);$$

and it can be oxidized to the monobasic *maltobionic acid*, $C_{12}H_{22}O_{12}$, hydrolyzable to dextrose and *d*-gluconic acid, $CH_2OH \cdot (CHOH)_4 \cdot COOH$.

These properties indicate maltose to contain only one of the two active groups present in two molecules of dextrose, for it forms an osazone with two molecules instead of four molecules of phenylhydrazine, and yields a monobasic acid instead of a dibasic acid. The process of union of the two molecules of dextrose must affect the active group of one molecule only. Such a connexion between two monose molecules is termed a *monocarbonyl-bond*. Denoting it by the sign $<$, and a free active group in a molecule by $\diagup$, maltose can be represented by

$$\underset{\text{Dextrose residue}}{C_6H_{11}O_5} < O \cdot \underset{\text{Dextrose residue}}{C_6H_{11}O_5}\diagup .$$

Lactose.

215. *Lactose* (*milk-sugar*) is present in milk, and is prepared from it.

Usually *whey* is employed for this purpose, it being the liquid remaining after the cream has been separated and the skimmed milk has been employed for making cheese. In these processes the milk is deprived of most of its fats and proteins, the whey containing nearly all the lactose and a large proportion of the mineral constituents of the milk. The lactose is obtained by evaporation, and is purified by recrystallization.

Lactose crystallizes in well-defined, large, hard crystals. It has not such a sweet taste as sucrose, and in the mouth resembles sand on account of the hardness of its crystals.

Hydrolysis transforms lactose into *d*-galactose and dextrose. It reacts as a monose, and can be proved by a method analogous to that employed for maltose to contain one free active group in the molecule, being therefore a product of the union of dextrose and *d*-galactose through a monocarbonyl-bond. The free active group belongs to the dextrose molecule, lactose being convertible by oxidation with bromine-water into *lactobionic acid*, a substance transformed by hydrolysis into *d*-galactose and *d*-gluconic acid. Accordingly lactose is represented by

$$\underset{\text{}d\text{-Galactose residue}}{C_6H_{11}O_5} < O \cdot \underset{\text{Dextrose residue}}{C_6H_{11}O_5}\diagup .$$

Sucrose.

216. *Sucrose* (*cane-sugar* or *saccharose*) is present in many plants, and is prepared from sugar-beet and sugar-cane. It crystallizes well,

and is very soluble in water. It melts at 184°, and on cooling solidifies to an amorphous vitreous mass, crystallizing after a considerable time. Crystallization from methanol yields a metastable modification melting at 170°. Strong heating turns it brown, owing to the production of *caramel*. Hydrolysis converts sucrose into dextrose and lævulose in equal proportions. This mixture is termed *invert-sugar*, and is lævorotatory, for at the ordinary temperature lævulose rotates the plane of polarization more to the left (209) than dextrose rotates it to the right. Sucrose is strongly dextrorotatory, the sign of the rotation being reversed by hydrolysis. This phenomenon is designated *inversion*, a term applied also to the hydrolysis of other dioses and of polyoses. Sucrose does not show the reactions characteristic of the monoses, for it does not reduce an alkaline copper solution, is not turned brown by potassium hydroxide, and does not yield an osazone. This lack indicates the absence of free active groups from its molecule, both of them being assumed to have reacted in the union of the two monoses. Such a linking between two monoses is termed a *dicarbonyl-bond*, and is represented by the sign $<O>$, sucrose having the formula

$$\underset{\text{Dextrose residue}}{C_6H_{11}O_5}<O>\underset{\text{Lævulose residue}}{C_6H_{11}O_5}.$$

With bases sucrose forms substances termed saccharates, that obtained from lime having the formula $C_{12}H_{22}O_{11},CaO,2H_2O$. This product is very soluble in water, and boiling its solution precipitates the nearly insoluble tricalcium saccharate, $C_{12}H_{22}O_{11},3CaO,3H_2O$.

Manufacture of Sucrose from Sugar-beet.

217. Sucrose is manufactured from sugar-cane and from sugar-beet, being present in solution in the cell-juice. Sugar-cane is cultivated in British India, in Java, in Cuba, in the south of the United States of America, and in other tropical countries. The cane is crushed between heavy iron or steel rollers, the expressed juice being worked up for the sugar by a process very similar to that employed with sugar-beet.

The cell-walls of the sugar-beet are lined with a thin continuous layer of protoplasm, constituting a semi-permeable membrane and preventing the diffusion of the sugar from the cells at the ordinary temperature. When placed in water at a temperature between 80° and 90°, the protoplasm is killed, coagulates, and develops minute ruptures permitting diffusion of the cell-fluid. The process is facilitated by cutting the beet into pieces between two and three millimètres in thickness. To make the diffusion-process as complete as possible with a

minimum amount of water, the slices are placed in vats with water circulating so as to bring the nearly exhausted material into contact with fresh water, that only partly exhausted being immersed in the solution already obtained. The effect is to maintain contact between the material richest in sugar and the strongest extract, and *vice versa* (principle of the counter-current). The solution obtained contains between twelve and fifteen per cent. of sugar, or about the proportion contained in the beet itself.

Slaked lime is added to this solution, whereby a double object is attained. First, the free acids in the juice, such as oxalic acid and citric acid, are precipitated along with the phosphates, their removal being necessary to prevent inversion on concentrating the solution. Second, proteins and colouring matters are precipitated from the solution. To accomplish these objects, it is necessary to add an excess of lime, part going into solution as saccharate. The saccharate is decomposed by a current of carbon dioxide, care being taken to maintain faint alkalinity of the liquid. The precipitate is separated by a filter-press, and the filtrate is concentrated. The maximum yield of sugar requires concentration at a low temperature, effected by boiling the sugar-solution under diminished pressure in vacuum-pans. The first product of the concentration is a thick syrup, more strongly alkaline than the original solution. Calcium carbonate is precipitated by the repeated action of carbon dioxide until the thick syrup is almost neutral. After filtration, the syrup is concentrated until crystals of sugar begin to separate. It is then allowed to cool, and more crystals mixed with a syrupy liquid removable by centrifuging are obtained. This syrup is crystallized further by slow agitation with a stirrer, the crystals being separated by means of the centrifuge. The residual syrup or molasses is utilized in the preparation of alcohol.

The sugar produced is not pure, being brown and containing a proportion of syrup. The crude material is purified by decolorizing its solution with animal-charcoal, and concentrating in vacuum-pans.

Quantitative Estimation of Sucrose.

218. The great practical importance of sucrose makes it desirable to have a quick and accurate method of estimating it quantitatively. This operation is effected almost exclusively by examining its aqueous solution with the polarimeter (**26**, 2). Sucrose is strongly dextrorotatory, its specific rotatory power being $(\alpha)_D = +66{\cdot}5°$. This expression means that, were it possible to prepare a solution containing 100 per cent. of sucrose, its rotatory power measured in a tube 100 mm. in length

would be $+66{\cdot}5°$. The rotatory power of a solution of one per cent. strength is therefore $+0{\cdot}665°$, and it is almost independent of the temperature. For practical purposes it can be taken to be proportional to the concentration. Obviously this method will yield accurate results only in the absence from the solution of other optically active substances. If present, such substances must be removed, or their effect must be taken into account. The first method is adopted in the determination of the amount of sugar in cane and in beet. The sample is grated with a fine rasp to destroy the cell-walls, and a weighed quantity is diluted to a certain volume with cold water, not only the sucrose but also optically active proteins being dissolved. These nitrogenous constituents and any colouring-matter present are precipitated by addition of basic lead acetate, the solution of sucrose filtered, and the amount of rotation observed.

When there is in the solution another sugar along with the sucrose, it is necessary to proceed by the second method. Suppose dextrose to be the other sugar present. The rotatory power of the dextrorotatory solution is determined first. Inversion of the solution will cause it either to diminish in dextrorotation or to become lævorotatory, since invert-sugar is lævorotatory. The rotatory power of an invert-sugar solution obtained from a sucrose solution of given strength being known, these two observations furnish the data for calculating the percentage of dextrose in the cane-sugar or the beet-sugar.

Velocity of Inversion of Sucrose.

219. The equation for unimolecular reactions (95) can be applied to the inversion of a dilute solution of sucrose. The original amount of the sugar being p, and the quantity inverted after a given time being x, the velocity s in the fraction of time immediately following can be expressed by the equation

$$s=\frac{dx}{dt}=k(p-x),$$

k being a constant. The inversion can be effected by means of different acids of the same molecular concentration. The velocity of the reaction being dependent on the nature of the acid employed, different values are obtained for the velocity-constant k.

Formerly proportionality was believed to exist between this constant and the concentration of the hydrogen ions; and in many instances, such as solutions of acid salts, it was customary to determine this concentration by measuring the velocity of inversion.

Closer investigation of the inversion of sucrose by means of acids has proved the process to be much more complex. Proportionality only exists when the acids are so dilute as to be ionized completely, under other conditions the ratio of the velocity-constant to the concentration of the hydrogen ions being dependent on the acid employed. In an example cited by Ostwald for seminormal acid-concentrations at 25° the ratio of k to the hydrogen-ion concentration for trichloroacetic acid is 1·98, but for acetic acid only 1·34. A more nearly constant value is obtained by assuming the undecomposed acid molecules to take part in the reaction, and introducing an appropriate correction.

The normal procedure for determining the velocity of inversion consists in the periodic measurement of the diminution of the rotation caused by the sucrose solution after the lapse of measured intervals of time, the process being tacitly assumed to accord with the simple scheme

$$\text{Sucrose} + \text{Water} \rightarrow \text{Dextrose} + \text{Lævulose}.$$

It is much more complex, for the α-dextrose liberated becomes partly transformed into β-dextrose (**208**), and most of the fructose produced changes to another form. Notwithstanding these facts, it is possible with a known concentration of sucrose and acid to obtain reasonably constant values for k, a phenomenon attributable to the great rapidity of these conversions.

Consideration of all these complexities is beyond the scope of this book, and it will suffice to examine the inversion of sucrose by the enzyme *invertase* (**222**).

With sucrose solutions of moderate concentration the amount of the sugar inverted is at first proportional to the time elapsed, twice as much

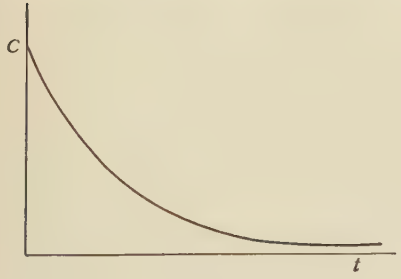


Fig. 59.—Inversion by Acids.

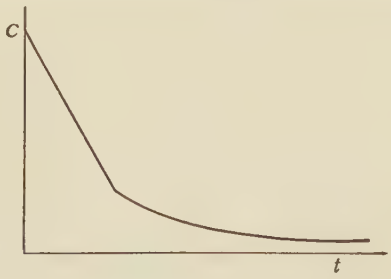


Fig. 60.—Inversion by Enzymes.

being transformed in $2n$ minutes as in n minutes. Only after the concentration of the sucrose solution has fallen below a certain limit does the transformation proceed in accordance with the law of unimolecular reactions, as with acids. To explain this phenomenon the invertase is assumed to unite primarily with only a portion of the sucrose present, the compound

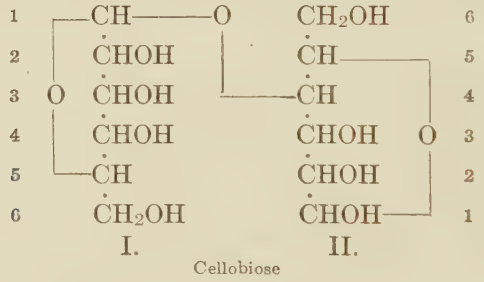
formed being alone susceptible of inversion. So long as there is excess of sucrose present, this product is formed repeatedly so as to maintain its concentration constant, and similar quantities of sucrose are inverted in like periods of time. As soon as the concentration of the sucrose has fallen too low for complete combination with the enzyme, the inversion proceeds in accordance with the law cited; for the proportion of the compound of sucrose and invertase no longer remains constant, but diminishes steadily until inversion has become complete.

The curves (Figs. 59 and 60) obtained by plotting periods of time as abscissæ and the concentrations of the sucrose solution as ordinates give a graphic representation of the inversion process.

Constitution of the Dioses.

220. Attention has been drawn (204) to the necessity for regarding the monoses as containing a closed chain of five carbon atoms and one oxygen atom. This grouping must be considered fundamental in all speculation on the constitution of the dioses. Two types of these compounds have been distinguished: in one the members exhibit reducing power and other characteristics of a free active group; in the other these properties are lacking.

Since the linking of the monose residues must be through oxygen, the following typical structural formula for a reducing diose is indicated:



Cellobiose

In this instance the active group is II, 1.

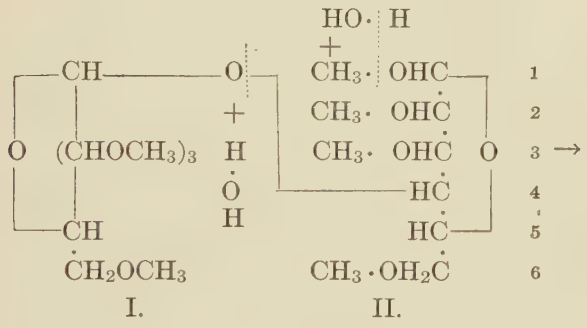
In respect of this formula the only arbitrary assumption made is the union of the two monose residues I and II through an oxygen-bridge from carbon atom 4 of II, the other hydroxyl-groups of II playing no part in this connexion. The presence of an active group in the diose excludes the possibility of hydroxyl-group II, 1 being concerned; and that of I, 1 must take part in the bridge, for the molecule lacks the additional active group otherwise essential. It remains to determine whether the monoses have the α-structure or the β-structure.

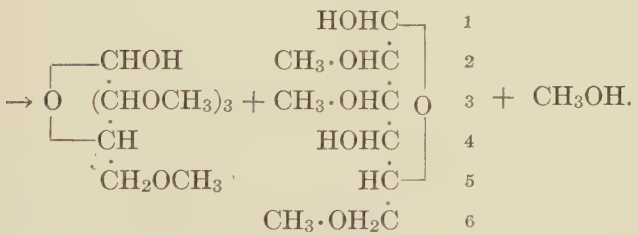
For a diose formed from two different monoses the problem of identi-

fying the monose to be represented by residue I, and that by residue II, must be solved. Its solution presents no serious difficulty, the method of oxidation employed for lactose having been indicated already.

For the reducing dioses the determination of the constitution of *cellobiose* and of maltose will be described, and for the non-reducing dioses that of sucrose.

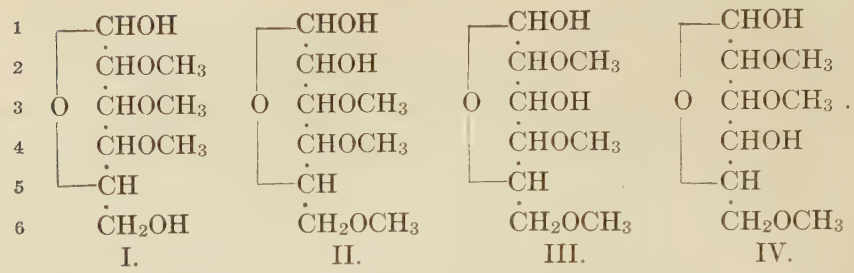
Cellobiose is a decomposition-product of *cellulose* (**227**), and can be proved to have the structure indicated by the formula. Methylation (**204**) replaces the hydrogen of each of the eight hydroxyl-groups by a methyl-group. Hydrolysis of this octamethyl-derivative by warming it with dilute hydrochloric acid hydrolyzes it to a mixture of tetramethyldextrose and trimethyldextrose:





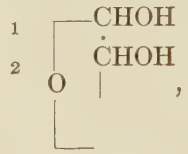
Part II of the octamethylcellobiose yields the trimethyldextrose, the methyl-group of its carbon atom 1 being readily eliminated (**204**, 3).

A difference in their solubility in chloroform affords a means of separating trimethyldextrose and tetramethyldextrose. The tetramethyl-compound is identical with the product of the methylation of free dextrose. The free hydroxyl-group of the trimethyldextrose must have been produced by the hydrolysis of the cellobiose, and identification of the carbon atom united with this group would reveal the mode of union of the monoses in cellobiose. It is possible to have four isomerides of a trimethyldextrose with a free active group:



I. II. III. IV.

A substance with formula II would be able to form an osazone on account of the presence of the group



and the failure of trimethyldextrose to exhibit this reaction excludes formula II.

Isomeride I is also excluded, for oxidation of trimethyldextrose with nitric acid eliminates a methoxyl-group, with formation of the dibasic *dimethylsaccharic acid,*

$$COOH \cdot CHOCH_3 \cdot CHOCH_3 \cdot CHOH \cdot CHOH \cdot COOH,$$

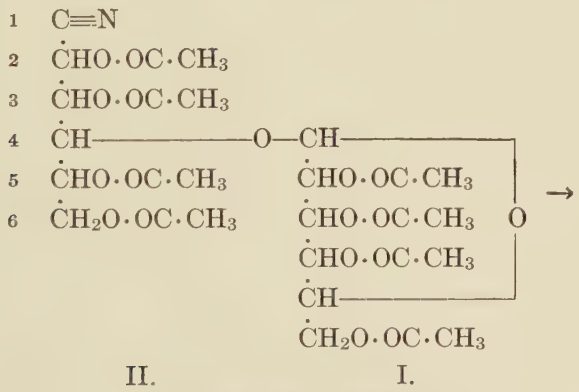
a substance capable of isolation as ethyl ester.

Isomerides III and IV have a terminal methoxyl-group, and obviously IV expresses the constitution of trimethyldextrose. The methoxyl-groups of this substance are therefore located at positions 2, 3, and 6.

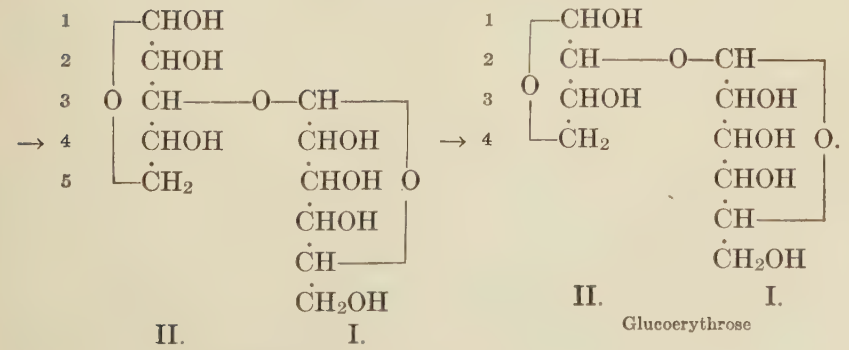
This structure can also be derived from that of lactose. This diose can be methylated to a heptamethyl-compound convertible by hydrolysis into a trimethyldextrose identical with that obtained from heptamethyl-cellobiose. The galactose residue of lactose is known to be in union with either group 5 or group 4 of the dextrose residue. As is indicated in **215**, the active group of lactose is combined with the dextrose residue, proving the galactose residue not to be in union with carbon atom 1. Moreover, lactose can yield an osazone involving its dextrose residue, indicating the presence of a free hydroxyl-group at carbon atom 2 next to the active group at 1. Oxidation of lactose yields lactobionic acid, and further oxidation converts this acid into a galacto-arabinose readily transformed into an osazone, a reaction indicating the presence of a free hydroxyl-group in union with carbon atom 3 of the dextrose residue. Consequently the galactose residue of lactose cannot be in union with carbon atoms 1, 2, or 3 of the dextrose residue, but must be attached to either 4 or 5. The epoxy-oxygen atom of the dextrose residue is united with carbon atom 1, and must also be linked with either 5 or 4. A trimethyldextrose with one of its methoxyl-

groups at carbon atom 6 must have its other two methoxyl-groups at positions 2 and 3.

An entirely different method of demonstrating the union of the two dextrose residues in cellobiose to be between carbon atoms I, 1 and II, 4 has been indicated by Zemplèn. Acetylation of cellobiose oxime yields a crystalline octa-acetylcarbonitrile of cellobionic acid, the process involving the transformation of the oxime group into a carbonitrile group by elimination of water. Sodium methoxide removes the acetyl-groups from this compound, and simultaneously replaces the cyano-group by a hydroxyl-group with formation of sodium cyanide, the product of the reaction being *glucoarabinose*, a diose with one carbon atom less than its parent substance. This diose yields an osazone, proving the adjacency of a CHOH-group to the active group. An analogous process transforms this glucoarabinose into a *glucoerythrose* incapable of forming an osazone, a proof of the lack in this glucoerythrose of a CHOH-group adjoining the active group:



Octa-acetylcarbonitrile of cellobionic acid



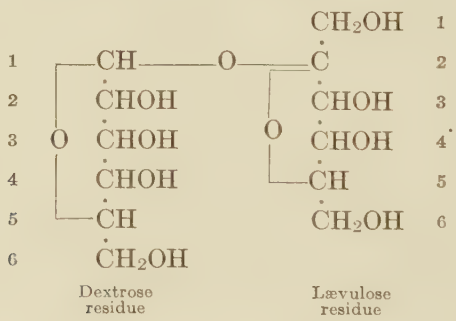
Obviously in this glucoerythrose the dextrose residue is in union with carbon atom 2 of the erythrose residue, consequently in the octa-acetylcarbonitrile of cellobionic acid the bridge-oxygen atom must be united with carbon atoms II, 4 and I, 1. The dextrose residues in cellobiose itself must therefore be connected by means of carbon atoms II, 4 and I, 1.

Analogous investigations have proved maltose to have the same structure as cellobiose, the only constitutional difference between the two sugars being the α-glucosidic linking of the two dextrose residues in maltose and the β-glucosidic linking in cellobiose.

The next problem is to determine whether the two dextrose residues in maltose are α or β. This carbohydrate is hydrolyzed by maltase, which attacks α-glucosides; it is unaffected by emulsin, which decomposes β-glucosides. It follows that carbon atom 1 of residue I must have the α-configuration, maltose being a dextrose-α-glucoside. The augmenting mutarotation exhibited by maltose constitutes a resemblance to β-dextrose, indicating carbon atom 1 of residue II to have the β-configuration. These facts prove maltose to be an α-glucoside of β-dextrose, and serve to establish its structure completely.

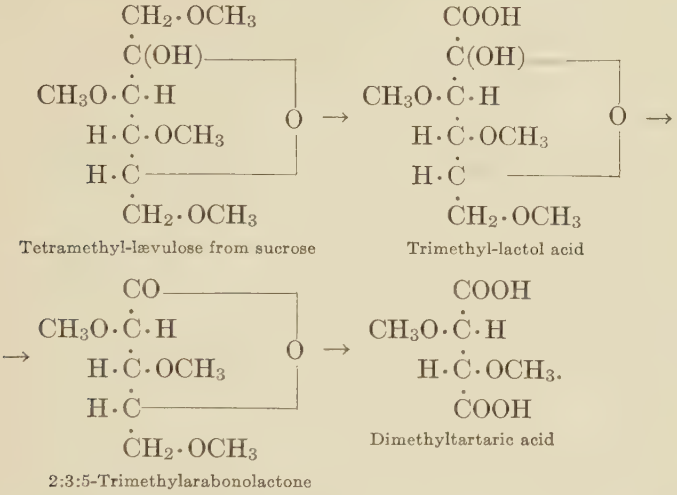
By analogous reasoning the β-glucosidic structure has been assigned to cellobiose.

The fact of sucrose having a dicarbonyl-bond indicates the union through oxygen of carbon atom 1 of dextrose and carbon atom 2 of lævulose, and for sucrose the structural formula



This formula accords with the transformation of sucrose by methylation with dimethyl sulphate and alkali into an octamethyl-derivative convertible by hydrolysis into ordinary tetramethyldextrose. These facts indicate the dextrose residue of sucrose to have the normal structure, but the lævulose residue is abnormal. The subjoined proof of the union of the epoxy-oxygen with carbon atoms 2 and 5 of the lævulose residue has been demonstrated by HAWORTH.

The oxidation of *tetramethyl-lævulose* obtained from sucrose yields a *trimethyl-lactol acid*, one of the CH_2OCH_3-groups becoming oxidized to carboxyl. Further oxidation degrades this compound to 2:3:5-*trimethylarabonolactone*, and the previously determined structure of this substance is confirmed by its oxidation to *dimethyltartaric acid*:



From these experiments emerges the remarkable fact of free lævulose having a structure (**209**) different from that possessed by it when combined in sucrose. A similar phenomenon characterizes inulin, whose lævulose residues have the same constitution as in sucrose, since methylation and hydrolysis produce the same tetramethyl-lævulose from it.

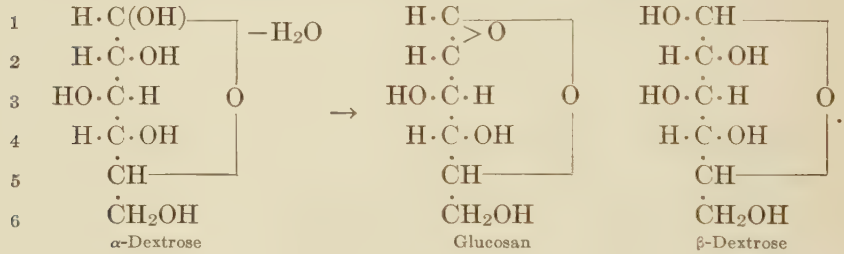
In researches of this type it is imperative to be able to ascertain the number of methoxyl-groups in the derivatives produced. The operation is effected by ZEISEL'S method of heating with a concentrated solution of hydrogen iodide, the methyl-groups in union with oxygen yielding methyl iodide. The amount of silver iodide obtained from this halide by the action of silver nitrate can be determined.

Synthesis of the Dioses.

For many years experimenters have sought to synthesize the natural dioses. Although in a few instances success has been attained by BOURQUELOT'S enzyme method, and some dioses not found in nature have also been synthesized, the problem for the commoner sugars, such as maltose, lactose, sucrose, and certain others, was solved only recently by PICTET by a method as ingenious as it is simple.

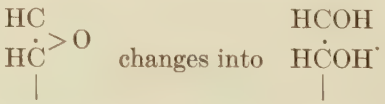
Maltose.—As already indicated, this diose is an α-glucoside of β-dextrose. It occurred to PICTET to heat in a vacuum at 150° a mixture in equal proportions of α-dextrose and β-dextrose. Water-vapour is evolved, and after cooling in vacuum a vitreous, congealed mass remains. Alcohol of 90 per cent. strength dissolves the unchanged β-dextrose remaining in the product, and addition of alcohol to a solution of the residue in water gives a precipitate of polyoses. After transformation by means of acetic anhydride of the substance remaining in solution, and repeated crystallization of the acetate, maltose octa-acetate is obtained in a state of purity. Careful saponification of this substance with sodium methoxide yields synthetic maltose identical with the natural product.

When α-dextrose is heated by itself at the same temperature, it loses one molecule of water with formation of *glucosan*, $C_6H_{10}O_5$. Under similar conditions β-dextrose does not lose water. This behaviour is explained by the stereochemical structure of the two dextroses (337):

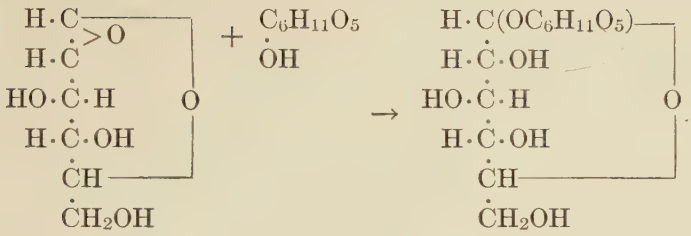


I. II. III.

Only formula I has two adjacent hydroxyl-groups on the same side of the carbon chain, these groups being capable of ready interaction. The elimination of water is assumed to be from the hydroxyl-groups at 1 and 2, and not from those at 1 and 3 or 4; and this view is confirmed by transforming glucosan into its trimethyl-derivative, and boiling this product with water. In this reaction one molecule of water is added, forming a reducing sugar convertible into an osazone, and therefore with a CHOH-group adjacent to the active group:



The first step in the synthesis of maltose must be assumed to be the formation of glucosan by heating α-dextrose, this reaction being followed by the addition of a molecule of β-dextrose;



Confirmation of this view of the mechanism of the process is obtained by heating equimolecular amounts of glucosan and β-dextrose at only 130° in presence of a small proportion of zinc chloride. Twice the quantity of maltose is produced, and there is no elimination of water.

Lactose.—An analogous process for synthesizing lactose involves the fusion at 175° in a vacuum of a mixture of equimolecular amounts of β-galactose and β-dextrose, the theoretical proportion of water,

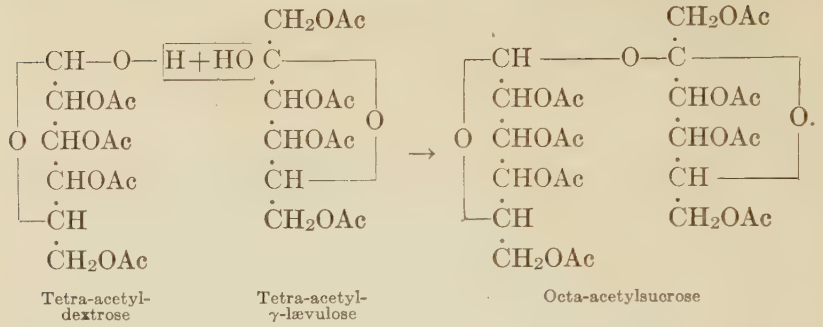
$$2C_6H_{12}O_6 - H_2O,$$

being eliminated.

Sucrose.—The synthesis of sucrose cannot be effected so directly, because the form of lævulose constituting part of that diose, with the epoxy-oxygen in union with carbon atoms 2 and 5, is unstable in the free state (compare 209 and the formula for sucrose on page 260). There are certain stable derivatives of this form, among them a tetra-acetyl-compound. When ordinary lævulose with its epoxy-oxygen in union with carbon atoms 2 and 6 is acetylated, the normal tetra-acetate crystallizes as the main product. Simultaneously there is produced a small proportion of an isomeride in syrup form, apparently the tetra-acetate of the unstable γ-modification. The experiment indicates lævulose in solution to be a mixture consisting of a large proportion of the stable form and a small proportion of the unstable variety.

A proof of the formation of the acetate of unstable lævulose is furnished by the union of this acetate with that of dextrose to form an octa-acetate of sucrose through elimination of water. The reaction is induced by dissolving the two acetates in chloroform, and agitating the solution with phosphoric oxide, P_2O_5.

Saponification of its octa-acetate yields sucrose identical with the natural product. In the subjoined scheme the acetyl-group is denoted by Ac:



Tetra-acetyl-dextrose — Tetra-acetyl-γ-lævulose — Octa-acetylsucrose

Numerous examples of diose production by the union of two monoses with elimination of water are possible, but it is most remarkable how only those corresponding with the formation of natural products have been induced. In the synthesis of sucrose chance plays a part, for the solution of ordinary lævulose contains the γ-form, and not one of the isomeric varieties possible with the epoxy-oxygen in union with other carbon atoms.

The syntheses of maltose and lactose are characterized by many more possible variations. A fortuitous fact of primary importance is the union of β-dextrose with the oxygen attached to carbon atom 2, and not with that linked to carbon atom 1. In addition, β-dextrose has five hydroxyl-groups; and the fact of the epoxy-oxygen of dextrose reacting with the hydroxyl-group of carbon atom 4, and not with one of the other four hydroxyl-groups, is quite accidental.

Alcoholic Fermentation.

221. The process of alcoholic fermentation was known in antiquity, but for many centuries a clear insight into its mechanism was lacking, and was not gained until the second half of the nineteenth century. Two types of research must be distinguished in this connexion, the first being the cause of fermentation, and the second the process involved in the phenomenon.

During last century two contradictory explanations of the cause of alcoholic fermentation were suggested:

1. Liebig assumed the proteins introduced into a solution of sugar along with the yeast to undergo decomposition, the change inducing the transformation of the sugar into carbon dioxide and alcohol. At first he refused even to admit yeast to consist of living cells.

2. The investigations of CAGNIARD DE LA TOUR and those of SCHWANN, and PASTEUR'S subsequent brilliant researches in 1860, engendered the belief that the living yeast in propagating itself acted as the agent for transforming the sugar, the process being a physiological phenomenon involving a complex biological function of the yeast-cells.

In consequence of the great regard felt for his authority, LIEBIG'S hypothesis was accepted almost generally for some decades, and lost its prominence only as a result of the completely convincing proofs advanced by PASTEUR in support of his own point of view. At a later period defects in PASTEUR'S theory were revealed by the work of EDUARD BUCHNER, whose explanation of the cause of fermentation is accepted now as correct.

In accordance with PASTEUR'S theory, the process of fermentation is inseparable from the presence and propagation of yeast-cells. The inducement of fermentation without their presence effected by EDUARD BUCHNER has rendered it invalid. He triturated fresh yeast with sand, whereby the cell-walls were destroyed. Under great pressure yeast-juice was separated from the dough-like mass, the cells suspended in it being removed by filtration. BUCHNER proved in various ways the freedom of this yeast-juice from living cells and living protoplasm. One method was to kill the yeast by the action of acetone; the extract from the dead yeast can induce in a solution of sugar active fermentation like that obtained with living yeast. The fermentation is caused by a dissolved substance classed with the proteins on account of its properties, such as coagulation on warming. It is a type of enzyme named by BUCHNER *zymase*. The yeast-cells have only the function of producing zymase.

The labour involved in the unravelling of the chemical process accompanying fermentation has not been less than that expended on the discovery of the cause of this fermentation.

LAVOISIER was the first investigator to undertake a quantitative study of the fermentation process, and about 1789 he came to the conclusion that it induced the transformation of sugar into alcohol and carbon dioxide without the taking up of water or of other substances. In 1813 GAY-LUSSAC suggested the representation of the reaction by the equation

$$C_6H_{12}O_6 = 2C_2H_6O + 2CO_2,$$

and in the main his view still is accepted as correct.

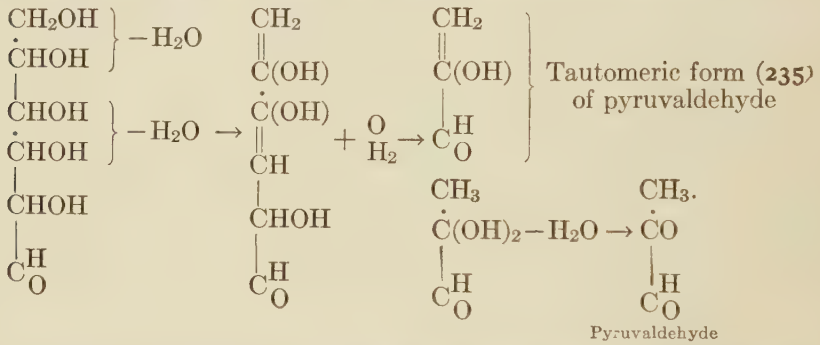
A mere comparison of the structure of sugar with that of carbon dioxide and that of alcohol indicates fermentation to be accompanied by an extremely complex transformation of the sugar molecules, probably involving various intermediate stages. A hypothesis suggested by VON BAEYER in 1870 constitutes the basis of the explanation proposed

by NEUBERG and at present accepted. VON BAEYER supposed the rupture of the sugar molecule to be preceded by a displacement of hydroxyl-groups and of hydrogen atoms, explicable on the assumption of a hydrogen atom undergoing transference after elimination of water in the ordinary way. The complex —CHOH·CHOH— is transformed first by loss of the elements of water into —CH:C(OH)—, this grouping then changing into —CH_2·CO—. The result is identical with that attainable by an exchange of position between hydrogen and hydroxyl, followed by elimination of water:

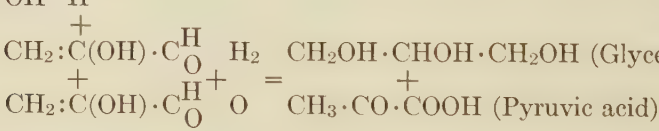
$$—CHOH·CHOH— \rightarrow —CH_2·C(OH)_2— \rightarrow —CH_2·CO—.$$

Various analogous transformations are known, among them the conversion of glycerol into acraldehyde (**152**).

After a change of the type indicated, the molecule is assumed to undergo fission into two parts, each with three carbon atoms:



According to this scheme the sugar molecule should yield two molecules of pyruvaldehyde. Since this substance is not fermentable, or at least can be fermented only very slowly, it cannot be an intermediate product in alcoholic fermentation, for that process at once yields carbon dioxide and alcohol. NEUBERG assumed two molecules of this aldehyde to react with water in accordance with CANNIZZARO's reaction (**108**):



Under the influence of yeast pyruvic acid is transformed very readily into acetaldehyde and carbon dioxide:

$$CH_3·CO·CO_2H = CH_3·C\overset{H}{\underset{O}{}} + CO_2.$$

The molecule of acetaldehyde thus generated reacts with one of pyruvaldehyde, with addition of a molecule of water:

$$\begin{array}{ccc} CH_3\cdot CO\cdot C\overset{H}{\underset{O}{}} & O & CH_3\cdot CO\cdot COOH \text{ (Pyruvic acid)} \\ + & + = & + \\ CH_3\cdot C\overset{H}{\underset{O}{}} & H_2 & CH_3\cdot CH_2\cdot OH \text{ (Ethyl alcohol)} \end{array}.$$

The regenerated pyruvic acid again is decomposed into carbon dioxide and acetaldehyde, this substance reacting with pyruvaldehyde as before. The cycle continues until the pyruvaldehyde has been consumed entirely. In yielding ethyl alcohol and carbon dioxide in equimolecular proportions, the process is in accord with Gay–Lussac's equation; and the accuracy of the explanation is supported by the formation of glycerol and acetaldehyde as by-products in alcoholic fermentation.

Very interesting evidence as to the course of fermentation has been obtained by Neuberg through addition of excess of sodium sulphite, Na_2SO_3, to a fermenting solution of dextrose. The effect was not to inhibit the fermentation process, but to generate quite different products, equivalent proportions of acetaldehyde as sulphite compound and of glycerol being obtained. Normally, the hydrogen taking part in the reaction is able to reduce the acetaldehyde to ethyl alcohol; and the explanation of the phenomena arising from the changed conditions lies in the inability of the sulphite derivative of acetaldehyde to undergo reduction, the hydrogen being consumed instead in the conversion of a molecule of pyruvaldehyde into glycerol.

During the war of 1914 to 1918 this method was employed in the manufacture of glycerol from dextrose (152).

Besides the alcoholic fermentation various other fermentation processes are known. Among them are the lactic and butyric fermentations of lactose; the putrefactive fermentation; and a number of others, examples already mentioned being the formation of butyl alcohol and acetone from starch (46 and 111), and that of citric acid from dextrose (197). The alcoholic fermentation of the amino-acids is considered in 242.

Fermentation processes are defined now as reactions initiated at the ordinary temperature and proceeding slowly, usually accompanied by the evolution of gas and by a positive calorific effect. In these processes micro-organisms such as yeast-cells, bacteria, moulds, and similar agents play a part analogous to that involved in alcoholic fermentation, generating the enzymes inducing the transformation.

Enzymes.

222. When present even in very small proportion, the substances known as *enzymes* have at the ordinary temperature the power of inducing reactions not otherwise initiated. They are true catalysts. Throughout the whole of organized nature they play a most important rôle, for without them life would be impossible. Among the typical instances of their action are the digestive processes of the animal economy. Saliva contains the enzyme *ptyalin*, capable of hydrolyzing starch. The enzyme *pepsin* is present in the stomach, and hydrolyzes proteins. In the pancreatic gland there are three enzymes: *lipase*, a hydrolyzer of fats; *amylase*, a hydrolyzer of polyoses; and *trypsin*, capable of decomposing proteins. In **43** mention is made of the ability of *diastase* to convert starch into maltose, and in **221** *zymase* is stated to be able to transform sugar into carbon dioxide and ethyl alcohol. More than a hundred enzymes are known at present. Such processes as the assimilation by plants of carbon dioxide and water (**223**) to produce starch, and the mineralization of vegetable or animal waste, must be regarded as enzyme actions.

Primarily the action of enzymes depends on the temperature, their activity being suspended below the freezing-point, but returning at the ordinary temperature. At temperatures between 30° and 50° it attains its maximum, but at higher temperatures the destruction of the enzyme diminishes it, none of them being able to withstand the temperature of boiling water. In great measure their action depends on the acidity of the solution, the *optimum* for invertase (see below) corresponding with

$$p_H = 4{\cdot}5 \text{ to } 5{\cdot}0.$$

A second characteristic of enzymes is their tendency to become inactive or "poisoned" through contact with small proportions of certain substances, among them hydrogen cyanide.

A third feature of the enzymes is the highly specific nature of their action, any individual being capable of inducing change in a few substances only, and exerting no influence on other similar compounds. This phenomenon is exemplified by the various monoses with two to ten carbon atoms, alcoholic fermentation being limited to the trioses, hexoses, and monoses. In accordance with their formula only these monoses can be converted readily into carbon dioxide and ethyl alcohol, a reaction typified by the scheme

$$n\mathrm{C_3H_6O_3} \rightarrow n\mathrm{C_2H_5OH} + n\mathrm{CO_2}.$$

The enzyme *invertase* present in yeast first transforms sucrose into dextrose and lævulose, these monoses then undergoing fermentation.

Formerly the fermentation of dioses was believed to require invariably a preliminary hydrolysis to monoses. Doubts as to the accuracy of this view have been engendered by the discovery of types of yeast containing little or no *maltase*, yet capable of readily fermenting maltose. There are also types of yeast, exemplified by *Schizosaccharomyces octosporus* discovered by Beyerinck, able to ferment maltose but not sucrose. Yeasts of this variety are assumed to lack invertase, but to contain the enzyme for the hydrolysis of maltose called maltase. For the rapid hydrolysis of each diose a specific enzyme is necessary, and each of these enzymes can induce other, but much slower, transformations.

The power possessed by enzymes of effecting decomposition was proved by Emil Fischer to be connected intimately with their stereochemical configuration. The three natural sugars, *d*-glucose, *d*-mannose, and *d*-fructose, can undergo fermentation; but their mirror-images, *l*-glucose, *l*-mannose, and *l*-fructose, are not fermentable.

Only incomplete insight into the chemical nature of the enzymes and their power of decomposing compounds has been attained. None has been isolated in the pure state, although in this respect in recent years great progress has been made through the researches of Willstätter and his collaborators. Initially he investigated the methods for extracting the enzymes from plants, glands, and other material, and found them to be susceptible of considerable improvement through judicious selection of the extracting liquid. One of his results demonstrated the alcoholic method formerly employed for extracting the pancreatic gland to be unsuitable in view of the destruction of the greater part of the enzymes, extraction with acetone being found to give good yields. He devised a method of determining the concentration of *enzyme* solutions involving measurement of the velocity of reaction induced by a known proportion of the solution under investigation.

The reactivity of a given quantity of a gland or of an enzyme solution can be expressed by two numbers, one giving the amount of enzyme present, and the other its activity. Each is measured in certain units, the first having been termed by Willstätter the *enzyme-unit*, and the second the *enzyme-value*. An example will make the procedure clear.

A small weighed portion of an enzyme preparation is added to a measured volume of a sucrose solution of known concentration, the *optimum* of p_H being maintained by the addition of a one per cent. solution of a primary phosphate. The time requisite for the reduction of the original rotation of the liquid to 0° is noted, this point corresponding with an inversion of about 75 per cent. of the sucrose. The number of minutes required to complete this operation was named by Willstätter the *time-value* of the solution, and the better the quality of the enzyme preparation the

smaller will this time be. He termed the inverse of the time-value the *enzyme-value*. The *enzyme-unit* is the quantity of enzyme in fifty milligrammes of the dry substance contained in the portion of the preparation added, and is given by the time measurement. For example, one saccharase-unit is present in (*a*) sixty grammes of fresh yeast, (*b*) fifteen grammes of dried yeast having the saccharase-value $\frac{1}{300}$, and (*c*) five milligrammes of a preparation with approximately the best saccharase-value, namely 10.

By determining the enzyme-value and the enzyme-unit at each stage of purification, the quality of the preparation can be judged; and by this means it is possible to control the step-by-step concentration of enzymes. The method is handicapped because the reactivity of the enzymes is often much affected by their degree of dispersion and by the nature of the associated substances. This phenomenon is specially characteristic of the lipolytic enzymes, but is much less marked with the enzymes employed in the hydrolysis of dioses.

In some instances, such as that of invertase from yeast, direct extraction was found to be impossible, the extraction of that enzyme by water requiring the preliminary destruction of the proteins by a proteolytic enzyme. This phenomenon points to the existence of a protective layer of proteins around the invertase.

Some enzymes appear to be combined with, or more probably adsorbed by, other substances present in the cells. *Emulsase*, the enzyme of bitter almonds, is extracted very imperfectly by water, but quite readily by an extremely dilute solution of an alkali.

The enzymes being chemically indifferent, chemical methods are inapplicable to their isolation. A general method for their concentration involves adsorption by aluminium oxide or kaolin, the substances most frequently employed by WILLSTÄTTER. They have a selective action, aluminium oxide adsorbing pancreatic lipase, but not the other enzymes of the pancreatic gland.

The experiments of WILLSTÄTTER have demonstrated the possibility of preparing various types of aluminium hydroxide of very divergent selective adsorptive power. He denoted these varieties as α, β, and γ. The α-modification is soluble in hydrogen-chloride solution of 0·1 per cent. strength, and in sodium-hydroxide solution of the same concentration; the γ-modification is insoluble in hydrogen-chloride solution of ten per cent. strength, and in sodium-hydroxide solution of four per cent. strength.

When precipitated aluminium hydroxide is heated with ammonia at 250°, a gel of the composition AlO·OH is produced. It lacks both basic and acidic properties, but is characterized by a high degree of selective adsorptive power.

The separation of the enzyme from the adsorbent can be effected by extraction with a suitable solution. For this purpose a dilute solution of a basic phosphate is employed frequently.

Sometimes difficulty is caused by the adsorbent precipitating also a considerable proportion of enzymatic indifferent substances, but in such instances the application of a second adsorbent carries the purification process a stage further. An example is furnished by the inability of kaolin to adsorb invertase of a certain degree of impurity, although it adsorbs purer specimens readily, leaving the contaminating yeast-gum in solution.

By these methods WILLSTÄTTER succeeded in raising the concentration of pancreatic lipase to three hundred times its concentration in the gland after removal of fat and water, and for yeast-saccharase he attained a concentration between sixteen and seventeen hundred-fold. Such a concentrated enzyme is free from proteins and carbohydrates, a fact refuting the view formerly adopted almost universally as to the enzymes being a type of protein. Its phosphorus content in this state does not exceed 0·006 per cent., indicating the impossibility of the enzyme containing numerous groups of nucleic acids.

Despite the great progress achieved, it is still impossible to isolate pure enzymes, and their chemical constitution remains unknown. The study of these substances is hampered by the great hindrances to obtaining them in the pure condition, as well as by the labour involved in isolating them in quantities adequate for chemical research.

Vitamins.

For many years the impossibility of maintaining life in animals fed with a mixture of purified albumin, fats, carbohydrates, and mineral substances has been known. These materials are the constituents of food. When young rats are fed on a mixture of this type, they die in a few days; but the addition of even a small proportion of milk to this diet keeps them healthy, and induces normal development. This effect must be due to the presence of milk of one or more substances, and research has demonstrated natural foodstuffs to contain in very small proportion products indispensable for health. They are termed *vitamins*.

The vitamins are classified in two varieties, those soluble in fats, and those soluble in water. Three of the first type are known, distinguished as *A*, *D*, and *E*. Vitamin-*A* and vitamin-*D* are present chiefly in liver-oil, and protect the body from the development of rickets. Animals fed on a diet lacking vitamin-*E* develop normally, except that they are sterile.

The saponification of fats with boiling caustic alkali leaves about one per cent. as an unsaponifiable residue. That from animal fats consists mainly of *cholesterol*, and that from vegetable fats of *phytosterol*, these substances being closely related, complex higher alcohols. Along with them are found the vitamins. Distillation of the mixture at a pressure of two millimètres yields a fraction containing the vitamins, and boiling between 180° and 200°, but it has not been possible to prepare them from this distillate in the pure state. When submitted to the action of ultraviolet light, both these sterols acquire the properties of vitamin-*D*. The proportion of vitamins essential for normal feeding during growth is extremely minute. It suffices to give rats receiving a daily food ration weighing fifteen grammes one-hundredth of a milligramme of the distillation fraction previously mentioned.

The vitamins soluble in water are denoted by *B* and *C*. Vitamin-*B* protects against beri-beri, vitamin-*C* against scurvy. Vitamin-*C* is present in greens, oranges, and lemons. C. Eykman detected vitamin-*B* in rice-bran, and after a lengthy series of experiments Jansen and Donath succeeded in the year 1926 in isolating it from this substance in the pure crystallized state. Pigeons fed on shelled rice sicken after about twelve days, but addition to their diet of one-millionth part of vitamin-*B* restores them to health. From 300 kilogrammes of rice-bran it is possible to prepare in the pure state about one-tenth of a gramme of the hydrochloride of this substance, a salt melting at 250°. Micro-analysis has indicated the provisional formula $C_6H_{10}ON_2$,HCl.

Asymmetric Synthesis.

223. Laboratory syntheses effected with optically inactive material always yield inactive compounds, but plants employ such inactive material as carbon dioxide and water for the synthesis of *d*-glucose and numerous other optically active compounds. They produce also optically active nitrogenous compounds, such as proteins and alkaloids, although the nitrogen reacts either in the free state or as nitric acid. Two problems present themselves for solution:

1. The mode of formation of the first optically active substance from inactive material.

2. The production of active substances from inactive material under the influence of an optically active body already existing.

The solution of the first problem is still unattained. The formation of the first optically active compound has been suggested to have been induced by the circularly-polarized light present at the earth's surface;

but although this hypothesis is plausible, it still lacks experimental confirmation.

More progress has been made towards the solution of the second problem, some asymmetric syntheses of this type having been effected, mainly by McKenzie and his coadjutors.

Reduction of *benzoylformic acid*, $C_6H_5 \cdot CO \cdot COOH$, yields inactive mandelic acid, $C_6H_5 \cdot CHOH \cdot COOH$. In contrast, reduction of an ester of this ketonic acid derived from such an optically active alcohol as the lævorotatory menthol produces a mixture of the ester of the dextro-acid with a small excess of that of the lævo-acid. Saponification gives active mandelic acid, despite the elimination of the asymmetric structure occasioned by the presence of the menthol residue. The formation of *l*-lactic acid by the reduction of *l*-bornyl pyruvate with aluminium-amalgam is a similar reaction:

$$\underset{\text{l-Bornyl pyruvate}}{CH_3 \cdot CO \cdot COOC_{10}H_{17}} \rightarrow \underset{\text{l-Lactic acid}}{CH_3 \cdot CHOH \cdot COOH}.$$

Another example is the formation of excess of *l*-tartaric acid through oxidation of monobornyl fumarate by permanganate (**324**).

In an analogous way the photosynthesis of dextrose from carbon dioxide and water under the influence of the optically active chlorophyll, a substance indispensable for the formation of starch in the plant, can be assumed to involve the formation of dextrose instead of inactive glucose.

The occurrence in nature of all the possible optical isomerides of a compound is exceptional. Only the dextrorotatory forms of dextrose, tartaric acid, and lactic acid are natural products. The reason for nature not having produced the chemical mirror-images of all optically active substances found in the existing flora and fauna is an unsolved problem, for so far as is known at present the probability of the formation of both types must have been equal.

III. POLYOSES.

Raffinose, $C_{18}H_{32}O_{16},5H_2O$.

224. *Raffinose* is the most important of the small group of hexotrioses. Their formula is $C_{18}H_{32}O_{16}$, or $3C_6H_{12}O_6 - 2H_2O$.

Raffinose is classed as a hexotriose, the hydrolysis of its molecule adding two molecules of water with formation of one molecule of lævulose, one of

dextrose, and one of *d*-galactose. Careful hydrolysis transforms raffinose quantitatively into lævulose and the diose *melediose*. This diose is different from lactose, but like it yields dextrose and *d*-galactose. The action of emulsin converts raffinose into *d*-galactose and sucrose. Raffinose does not exhibit any of the monose reactions, this characteristic being exemplified by its inability to reduce an alkaline copper solution. This lack proves the absence of an active group, raffinose being represented by

$$C_6H_{11}O_5{<}O{\cdot}C_6H_{10}O_4{<}O{>}C_6H_{11}O_5.$$

Melediose has the sugar reactions, and therefore contains one free active group, its formula being

$$C_6H_{11}O_5{<}O{\cdot}C_6H_{11}O_5{<}\diagup.$$

These facts indicate the decomposition of raffinose into monose and diose to occur at the dicarbonyl-bond, as otherwise there would be obtained a diose, $C_6H_{11}O_5{<}O{>}C_6H_{11}O_5$, lacking a free active group.

Raffinose crystallizes with five molecules of water. Sucrose containing a certain proportion of this polyose yields pointed crystals.

Manneotetrose is a tetrose present in manna. Hydrolysis of its molecule yields two molecules of galactose, one molecule of dextrose, and one molecule of lævulose:

$$\underset{\text{Manneotetrose}}{C_{24}H_{42}O_{21}}+3H_2O=\underset{\text{Galactose}}{2C_6H_{12}O_6}+\underset{\text{Dextrose}}{C_6H_{12}O_6}+\underset{\text{Lævulose}}{C_6H_{12}O_6}.$$

Higher Polyoses.

225. Most of the higher polyoses are amorphous, and do not possess a sweet taste; many of them are insoluble in water. Their hydrolysis yields monoses, either pentoses or hexoses, indicating the monose residues to be united through the oxygen atom. The molecular weight of the polyoses is unknown, but it must be very great. Their empirical formula is $C_6H_{10}O_5$. Hydrolysis of nearly all the polyoses yields monoses with the same number of carbon atoms.

Starch.

Starch is the first observable assimilation-product of plants. It occurs in large quantities in the tubers, roots, and seeds of many plants, being present in the form of granules differing in form and size in different plants. Some of these granules are represented in Figs. 61, 62, and 63.

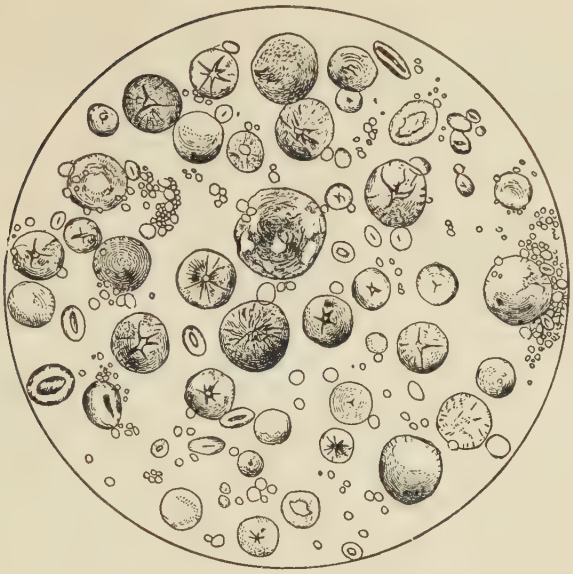


FIG. 61.—RYE-STARCH. × 320.

Starch is insoluble in cold water, and in hot water it swells without dissolving. It yields an intense blue coloration with a dilute solution of iodine, the reaction serving as a test for both this halogen and starch.

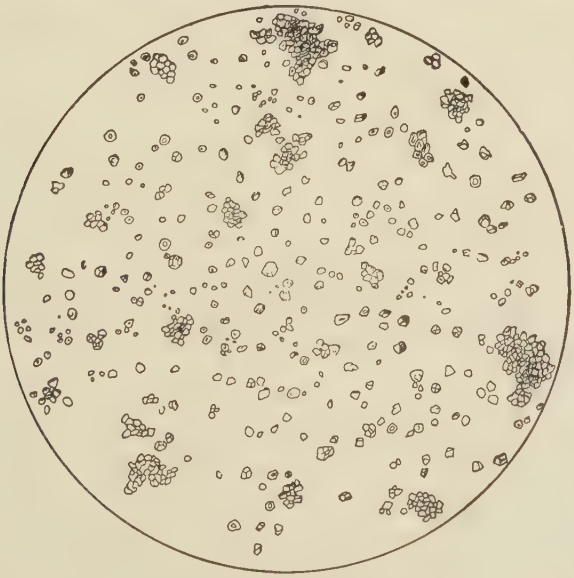


FIG. 62.—RICE-STARCH. × 320.

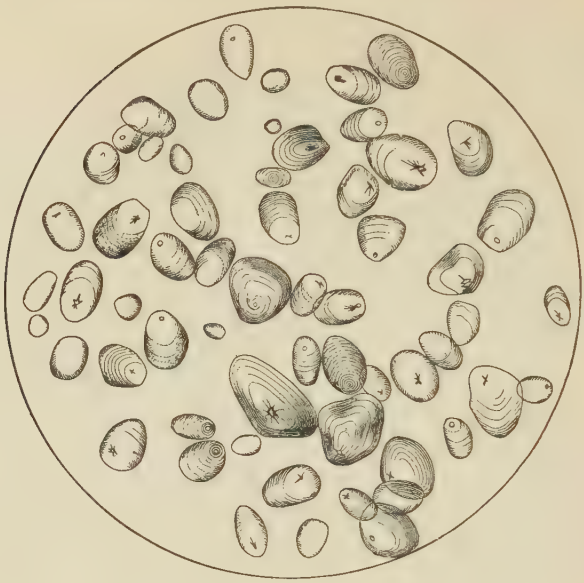


FIG. 63.—POTATO-STARCH. × 250.

Addition under the microscope of a concentrated solution of tannin to the liquid obtained by boiling one gramme of potato-starch with 100 c.c. of water demonstrates the starch-granules to consist of a skin filled with a liquid coagulated by the action of the tannin. Starch consists therefore of two distinct individuals: the skin, designated *amylocellulose*; and the soluble part, termed *granulose*. Amylocellulose constitutes about eighty-three per cent. by weight of starch, and can be prepared from it by extraction of the granulose with a dilute solution of sodium hydroxide. Only the granulose produces the blue coloration with iodine.

Boiling with dilute acids converts starch completely into dextrose. Contact with diastase induces liquefaction of starch-paste, followed by decomposition of its molecules with ultimate formation of maltose and *iso*maltose, $C_{12}H_{22}O_{11}$. Each process yields intermediate gum-like polyoses termed *dextrins*, and having a smaller number of atoms in the molecule than starch. Some of these products have been obtained in crystalline form. Dextrins are formed also by heating starch alone at 200°, or with a small proportion of nitric acid at 110°.

An amorphous flocculent precipitate of dextrins is obtained through addition of alcohol to their aqueous solutions. Unlike starch, they give a red coloration with a solution of iodine. Addition of cold concentrated hydrochloric acid to starch causes considerable swelling of the granules, and the production of a thick jelly. After the lapse of a few

hours the jelly liquefies, the starch having undergone conversion into dextrin. The transformation is proved to have occurred by the red coloration given with iodine, and by the amorphous flocculent precipitate deposited through addition of alcohol. At the end of a few days neither of these dextrin reactions can be obtained, and the solution is found to contain dextrose only.

Different plants not only contain starch and dextrin in different proportions, but these constituents differ in such properties as solubility.

Starch lacks the reactions of the monoses, this characteristic being exemplified by its inability to reduce an alkaline copper solution, to undergo resinification by alkalis, and to yield a compound with phenylhydrazine. These facts prove the absence of a free carbonyl-group.

Manufacture of Starch.—The process for the manufacture of starch does not present any theoretical difficulties. Potato-starch is prepared by fine grinding of potatoes to destroy the cell-tissue and lay bare the starch-granules. These granules are washed from the cell-tissue by the action of water in a special apparatus somewhat resembling a sieve. They are allowed to settle, are washed carefully, and dried slowly.

Starch is employed for many purposes in the arts, as an adhesive paste, and for stiffening linen in laundries. In the laundry process the starch-paste is converted by the heat of the smoothing-iron into a stiff and glossy layer of dextrin coating the fibres of the linen. Starch is of great importance as a constituent of foods, its utility in this connexion being considered more fully in physiological text-books.

Glycogen $(C_6H_{10}O_5)_x$.

Glycogen is a substance resembling starch, and is present in both moulds and yeast as well as in such an animal organism as that of oysters, whereas the other polyoses are vegetable products. Usually it is prepared from rabbit-liver by destroying the tissue with a boiling concentrated solution of an alkali-metal hydroxide, the glycogen being unaffected. It is a white amorphous powder, dissolving in water with formation of an opalescent solution. Its hydrolysis yields dextrose only.

Cellulose $(C_6H_{10}O_5)_x$.

226. *Cellulose* is a polyose of very high molecular weight. The cell-walls of plants consist principally of it and of *lignin*, a substance probably not a polyose.

Lignin can be separated from wood by dissolving the cellulose in a solution prepared by saturating hydrochloric acid at 0° with gaseous hydrogen chloride.

The formula of lignin is unknown, but it contains the groups methoxyl, acetyl, and formyl. The formation of methyl alcohol by the dry distillation of wood depends on the presence of lignin, the process not producing this alcohol from pure cellulose. Lignin also contains benzene-nuclei, for its oxidation at 400° by oxygen under pressure yields benzoic acid and metaphthalic acid (**350**). Similar oxidation of cellulose produces fatty acids and oxalic acid. A test for lignin is described in **228**.

Cellulose is very stable towards dilute acids and alkalis, a property utilized in the technical preparation of cellulose to free it from companion substances in the plant-material. *Linen*, *cotton*, and *paper* consist almost exclusively of cellulose, and good filter-paper is cellulose of a high degree of purity. Cellulose is hydrolyzed completely by dissolving it in concentrated sulphuric acid, diluting with water, and boiling the solution. The cellulose from such material as cotton-wool and paper yields dextrose exclusively, that from such products as coffee-beans and cocoa-nibs giving *d*-mannose. Cellulose is converted by sulphuric acid containing half its volume of water into a colloidal modification, *amyloid*, characterized by yielding a blue coloration with iodine. This reaction furnishes a test for cellulose. The ammoniacal solution of cupric oxide known as SCHWEITZER'S reagent dissolves cellulose, the polyose being precipitated chemically unchanged from this solution by acids and salts, and drying to an amorphous powder.

The action of acetic anhydride and concentrated sulphuric acid on the cellulose of filter-paper, of cotton-wool, and of other materials, yields the octa-acetyl-compound of the diose cellobiose (**220**), obtained by saponification of the acetyl-derivative with alcoholic potash. Inversion converts cellobiose into dextrose. It is the simplest polyose obtained from cellulose, as maltose is the simplest polyose formed from starch. This fact furnishes an important argument from the chemical standpoint, supported by observations in vegetable physiology, in favour of regarding cellulose and starch as essentially different substances, and against assuming cellulose to be a higher polymeric form of starch.

CONSTITUTION OF THE HIGHER POLYOSES.

227. For the higher polyoses also it will be necessary to limit the consideration of structure to two examples, but they will furnish sufficient insight into the procedure applicable to tracing the constitution of the other polyoses.

The formula of the dioses is $C_{12}H_{22}O_{11}$, these substances being produced by the elimination of one molecule of water from two monose molecules. By analogy with this type of reaction the formula of the polyoses was formerly believed to be capable of representation as

$$nC_6H_{12}O_6-(n-1)H_2O,$$

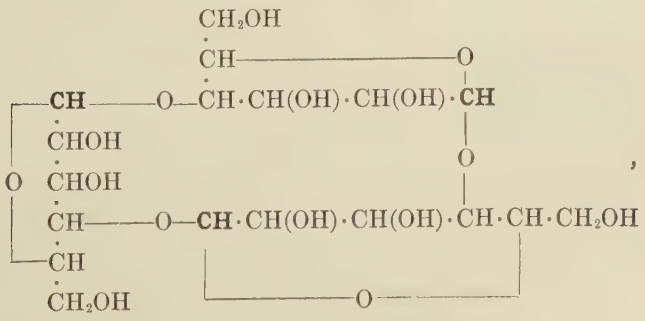
approximating as n increased to the empirical formula $C_6H_{10}O_5$ indicated by quantitative analysis. For various reasons this view is now known to be incorrect, one of them being the degradation of starch by the action of *Bacillus macerans*. The process yields definite crystallized compounds termed *amyloses* with the composition $(C_6H_{10}O_5)_3$ or $(C_6H_{10}O_5)_4$; and these substances exhibit many of the characteristics of starch, among them the formation of a coloration with iodine.

The current view assumes the polyoses to be produced by the removal of n molecules of water from n $C_6H_{12}O_6$ molecules, the elimination of water being attended by ring formation as exemplified in the subjoined formula for cellulose. This assumption is based on the following considerations. If the hexose residues were arranged in an open chain, there would have to be two terminal hexose residues each with four free hydroxyl-groups, each of the intermediate residues having only three such groups. The maximum number of methyl-groups capable of being introduced into the polyoses for each $C_6H_{10}O_5$-group is three, and hydrolysis of the methylated products yields exclusively trimethylglucose. With an open-chain structure small proportions of tetramethylglucose should also be obtained.

Cellulose.—As indicated previously, the degradation of the polyoses yields cellobiose, a logical reason for making the structure of this compound the basis for that of cellulose.

Elimination of a molecule of water from groups I, 6 and II, 1 of cellobiose, $C_{12}H_{22}O_{11}$ (**220**), gives the empirical formula $C_6H_{10}O_5$, that of cellulose. The compound produced has the formula $(C_6H_{10}O_5)_2$, and resembles cellulose in its lack of an active group, a characteristic corresponding with the absence of reducing power. These facts point to cellulose being a simple polymeride of the complex $(C_6H_{10}O_5)_2$. A difficulty is the failure to obtain a hundred per cent. yield of cellobiose, the maximum being fifty per cent.; but it is right to remember the great experimental difficulties associated with the process, for probably they inhibit the attainment of a theoretical yield.

It is therefore necessary to assume the complex to have at least three glucose-residues, the corresponding theoretical yield being sixty-six per cent. Actually a small proportion of a triose named *procellose* has been detected among the products of acetolysis. The structure of such a complex can be represented by the formula



the CH-groups in union with an active group after hydrolysis being indicated by bold-face type.

The additional possibility of the cellulose molecule being constructed of open chains composed of a great number of cellobiose residues cannot be wholly excluded.

Starch.—The methylation of starch readily substitutes two methyl-groups in each $C_6H_{10}O_5$-group, but only very prolonged methylation yields a product with 43·7 per cent. of OCH_3, corresponding with three methyl-groups for each $C_6H_{10}O_5$-group. Hydrolysis of this trimethyl-derivative of starch gives a good yield of the same 2:3:6-trimethyldextrose obtainable from maltose and cellobiose. These results and the formation of amyloses from starch justify the assumption of the basic complex of that substance being a trihexosan with the dextrose residues united between carbon atoms 1 and 4, as in the formula proposed for procellose. Whilst the linking of the dextrose residues in procellose is β-glucosidic, that in the trihexosan constituting the basis of starch must be α-glucosidic. The possibility of starch having a ring-structure of more than three dextrose residues must also not be overlooked.

Technical Applications of Cellulose; Nitrocelluloses; Artificial Silk.

228. *Linen* is prepared from the stalk of the flax-plant. The linen fibres can be obtained from the flax, cellulose being very stable towards chemical reagents. One method involves steeping the flax in water for a period between ten days and a fortnight. The consequent decay of the external fibre gives rise to an unpleasant smell. The material is dried by spreading in the open, and then is passed between corrugated rollers. This crushing loosens the external woody fibre, and it is stripped off by revolving wooden arms named "wipers," a process termed "scutching." The linen-fibres have a grey colour, and are bleached either by exposure to moist air and sunlight or by means of bleaching-powder.

Formerly *paper* was prepared almost exclusively from linen-rags, but now it is manufactured mainly from wood and straw. These materials must be divided into fibres, and the fibres are separated as much as possible from the other "incrusting" substances present. For wood this end is attained by the *sulphite-method* through heating under pressure with a solution of calcium hydrogen sulphite, and for straw by heating under pressure with sodium hydroxide. By these processes most of the incrusting substances are dissolved, the wood or straw being bleached at the same time. The residual cellulose can be separated readily into fine fibres, an operation necessary to the manufacture of paper-pulp. It is not possible to remove all the lignin by these means, and accordingly wood-paper and straw-paper answer the tests for lignin, and can be recognized thereby. Lignin gives a yellow coloration with salts of aniline (**297**), and a

red coloration with a solution of phloroglucinol (337) in concentrated hydrochloric acid.

Parchment-paper is prepared by converting the outer surface of paper into amyloid (226), a process imparting toughness to it.

The *nitrocelluloses* are of great technical importance. Cotton-wool is transformed by the combined action of nitric acid and sulphuric acid into a mixture of *mononitrocellulose*, *dinitrocellulose*, and *trinitrocellulose*, the extent of the nitration being dependent on the concentration of the acids and the duration of the process. Cellulose is assumed arbitrarily to have the molecular formula $C_6H_{10}O_5$.

The solution in a mixture of alcohol and ether of mononitrocellulose and dinitrocellulose is known as *collodion*. On evaporation it leaves an elastic skin, and it is employed in photography and in the manufacture of celluloid. Trinitrocellulose is *guncotton*, a substance resembling cotton-wool in appearance, but feeling somewhat rough to the touch. It is employed extensively as an explosive. On ignition a loose tuft burns readily, but it can be exploded by the detonation of a small proportion of mercuric fulminate, yielding only the gaseous products nitrogen, hydrogen, water-vapour, carbon monoxide, and carbon dioxide. It exerts a detonating or *brisant* (154) action, and without modification is unsuitable for artillery use.

Solution of guncotton in acetone or ethyl acetate gives a gelatinous mass, converted by removal of the solvent into an amorphous transparent substance with the same chemical composition as guncotton, but burning and exploding more slowly. This method of moderating the velocity of explosion of guncotton makes it available in this form for artillery purposes under the name "smokeless powder."

Artificial silk is manufactured by forcing a solution of cellulose through very narrow orifices immersed in a bath capable of reprecipitating the cellulose in lustrous threads resembling silk in appearance. Photographic film is made similarly, the orifices being replaced by a narrow slot.

On the manufacturing scale the cellulose is brought into solution by one of four processes: (1) by means of Schweitzer's reagent (226); (2) by preliminary nitration to mononitrocellulose and dinitrocellulose, and solution of these nitro-compounds in alcohol and ether, the threads being denitrified subsequently by the action of various reducers: (3) by conversion of the cellulose into a xanthate (264), a very thick liquid termed *viscose* being formed; (4) by transformation of cellulose into its triacetate by means of acetic anhydride, the triacetate being soluble in acetone. To coagulate the fibres, the solution obtained by the first method is pressed out into dilute acid; that produced by the second method into a large proportion of water; and that formed by the third method into a solution of ammonium sulphate or of dilute sulphuric acid.

AMINO-ALDEHYDES AND AMINO-KETONES.

229. Very few *amino-aldehydes* and *amino-ketones* are known. One of the most important is *chitin*. Apart from inorganic substances, it is the principal constituent of the shells of the crustacea, and is prepared either from the shell and claws of the lobster, or better from the shell of the shrimp. Chitin is also found in the vegetable kingdom, chiefly in the cell-walls of fungi.

When chitin is boiled with a concentrated solution of an alkali-metal hydroxide, it is decomposed with formation of acetic acid and a basic substance termed *chitosan*. A concentrated solution of hydrogen chloride converts chitosan almost completely into *glucosamine hydrochloride*, $C_6H_{13}O_5N,HCl$, a substance obtainable in well-defined crystals. The acetic acid and glucosamine are formed in equivalent proportions. When brought into contact with nitrous acid, glucosamine evolves nitrogen after the manner of primary amines and acid amides, an aldose being produced. This reaction indicates the probability of the acetyl-group being united with the nitrogen of an amide. Chitin can be regarded as a polymeride of an acetylaminoglucose, and as constituting a link between the proteins and cellulose.

ALDEHYDO-ACIDS AND KETONIC ACIDS.

Glyoxylic Acid, $COOH \cdot C\overset{H}{O} + H_2O$.

230. *Glyoxylic acid* is the first member of the series of aldehydo-acids. It is present in unripe fruits, and can be prepared by heating dibromoacetic acid, $CHBr_2 \cdot COOH$, with water, or by the electro-reduction of oxalic acid. It is also a product of the oxidation of alcohol with nitric acid by the method described under glyoxal (**198**).

As its formula indicates, glyoxylic acid contains one molecule of water, and this constituent cannot be separated from the acid or from its salts without their decomposition. For this reason the water often is assumed to be in chemical combination (**149**) as represented by the formula $CH(OH)_2 \cdot COOH$, analogous to that of chloral hydrate (**201**). In each of these substances the aldehydo-group, $-C\overset{H}{O}$, is under the influence of a strongly negative group; $-CCl_3$ in chloral, and $-COOH$ in glyoxylic acid. The acid also possesses all the properties characteristic of aldehydes, reducing an ammoniacal silver solution, forming an addition-product with sodium hydrogen sulphite, yielding an oxime, etc. Boiling with potassium hydroxide converts it into glycollic acid and oxalic acid, their formation being explicable by assuming one molecule of the acid to take up the two hydrogen atoms and another the oxygen atom from one molecule of water:

$$2COOH \cdot CHO \rightarrow COOH \cdot CH_2OH + COOH \cdot COOH.$$

Pyruvic Acid, $CH_3 \cdot CO \cdot COOH$.

231. *Pyruvic* (*pyroracemic*) *acid*, the first member of the series of ketonic acids, owes its second name to its formation by the distillation of either tartaric acid or racemic acid with potassium hydrogen sulphate. Probably carbon dioxide is eliminated first from tartaric acid,

$$COOH \cdot CHOH \cdot CHOH \cdot COOH,$$

with formation of glyceric acid, $CH_2OH \cdot CHOH \cdot COOH$, and this derivative yields pyruvic acid by the loss of one molecule of water, for glyceric acid is converted into pyruvic acid by heating with potassium hydrogen sulphate:

$$CH_2OH \cdot CHOH \cdot COOH - H_2O =$$

$$= CH_2{=}C(OH) \cdot COOH \rightarrow CH_3 \cdot CO \cdot COOH.$$

Pyruvic acid can be obtained synthetically by hydrolysis of the carbonitrile formed by the action of potassium cyanide on acetyl chloride:

$$CH_3 \cdot COCl \rightarrow CH_3 \cdot CO \cdot CN \rightarrow CH_3 \cdot CO \cdot CO_2H.$$

This type of reaction affords a general method for the preparation of 1-ketonic acids.

At 150° dilute sulphuric acid converts pyruvic acid into carbon dioxide and acetaldehyde:

$$CH_3 \cdot CO \cdot \boxed{CO_2}H = CH_3 \cdot C\overset{H}{\underset{O}{}} + CO_2.$$

At the ordinary temperature pyruvic acid is liquid, but it is solid at a low temperature. It melts at 9°, boils at 165°, and is miscible with water in all proportions. At 20° its density is 1·27. It has an odour resembling that of acetic acid. It is a stronger acid than propionic acid with 10^4k equal to 0·134; for pyruvic acid 10^4k is 56, a difference explicable by assuming the presence of a negative carbonyl-group in juxtaposition to the carboxyl-group.

Pyruvic acid has all the properties characteristic of ketones, yielding an oxime, a hydrazone, an addition-product with hydrogen cyanide, and so on.

Addition of boric acid to an aqueous solution of pyruvic acid causes a marked rise in the value of the electric conductivity of the organic acid. This phenomenon is characteristic of 1-hydroxy-acids (180), and indicates each molecule of pyruvic acid to be in union with one molecule of water, in accordance with the structural formula $CH_3 \cdot C(OH)_2 \cdot COOH$.

Acetoacetic Acid, $CH_3 \cdot CO \cdot CH_2 \cdot COOH$.

232. *Acetoacetic acid* is a 2-ketonic acid. It is not of much importance, but its ester *ethyl acetoacetate*, $CH_3 \cdot CO \cdot CH_2 \cdot COOC_2H_5$, is an interesting compound.

Ethyl acetoacetate is obtained by Claisen's condensation-method

(200) through the action of sodium on ethyl acetate in presence of ethyl alcohol:

$$CH_3\cdot C\overset{O}{\underset{OC_2H_5}{}} \rightarrow CH_3\cdot C\overset{ONa \quad H}{\underset{OC_2H_5 \quad H}{}}C\cdot COOC_2H_5 =$$

Ethyl acetate

Addition-product

$$= 2C_2H_5OH + CH_3\cdot C\overset{ONa}{}=CH\cdot COOC_2H_5.$$

Ethyl sodioacetoacetate

This explanation of the condensation was proved by Claisen to be correct. He demonstrated the impossibility of preparing ethyl acetoacetate by the action of sodium on ethyl acetate purified from alcohol. The free ester, $CH_3\cdot CO\cdot CH_2\cdot COOC_2H_5$, can be obtained from the sodium compound by acetic acid, for in the substitution of sodium by hydrogen the group —C(OH):CH— is formed first, and is transposed subsequently into —CO·CH_2— (131).

Ethyl acetoacetate is a colourless liquid, slightly soluble in water, and characterized by an agreeable odour. It boils at 181°, and at 15° has the density 1·030. It can be hydrolyzed in two ways, known on account of the nature of the products as the *ketone decomposition* (*weak hydrolysis*) and the *acid decomposition* (*strong hydrolysis*).

The ketone decomposition is effected by heating ethyl acetoacetate with dilute sulphuric acid, or with a dilute aqueous solution of alkali, the products being acetone, carbon dioxide, and alcohol:

$$\begin{array}{r|c|l} CH_3\cdot CO\cdot CH_2\cdot & & C_2H_5 \\ +H & CO_2 & OH \end{array} = CH_3\cdot CO\cdot CH_3 + CO_2 + C_2H_5OH.$$

The acid decomposition is induced by heating ethyl acetoacetate with a very concentrated solution of alcoholic potash or soda:

$$\begin{array}{r|c|l} CH_3\cdot CO\cdot & CH_2\cdot COO & C_2H_5 \\ +OH & H+H & OH \end{array} = CH_3\cdot COOH + CH_3\cdot COOH + C_2H_5OH.$$

The great importance of ethyl acetoacetate for synthesis arises from its capability of undergoing these two decompositions, and from the existence of a great many derivatives with one or two of the hydrogen atoms of the methylene-group, —CH_2—, replaced by substituents. Exchange of one or two hydrogen atoms for one or two groups R gives the compound

$$CH_3\cdot CO\cdot CHR\cdot COOC_2H_5 \quad \text{or} \quad CH_3\cdot CO\cdot CR_2\cdot COOC_2H_5,$$

convertible by the ketone decomposition into the ketone

$$CH_3 \cdot CO \cdot CH_2R \quad \text{or} \quad CH_3 \cdot CO \cdot CHR_2,$$

a reaction affording a general method of synthesizing methylketones (101).

The acid decomposition transforms the compounds

$$CH_3 \cdot CO \cdot CHR \cdot COOC_2H_5 \quad \text{and} \quad CH_3 \cdot CO \cdot CR_2 \cdot COOC_2H_5$$

into acetic acid and an acid with either the formula

$$CH_2R \cdot COOH \quad \text{or} \quad CHR_2 \cdot COOH,$$

the reaction furnishing a general method for the synthesis of monobasic acids.

The formation of such derivatives of ethyl acetoacetate involves the preliminary interaction of sodium ethoxide and the ester to form a sodium compound, $CH_3 \cdot C(ONa) : CH \cdot COOC_2H_5$ (235). Addition of an organic halide, R·X, X representing a halogen atom, gives the product

$$CH_3 \cdot \overset{\overset{ONa}{|}}{\underset{\underset{X}{|}}{C}} - - \overset{\overset{H}{|}}{\underset{\underset{R}{|}}{C}} \cdot COOC_2H_5.$$

Elimination of sodium halide, NaX, from this substance yields the compound $CH_3 \cdot CO \cdot CHR \cdot COOC_2H_5$, the hydrogen atom of its CHR-group being capable of analogous replacement.

233. A few examples of this synthetic method are appended.

1. *Methylnonylketone* or *undecanone*-2, the principal constituent of oil of rue (from *Ruta graveolens*), can be obtained by the action of *n*-octyl iodide on ethyl sodioacetoacetate:

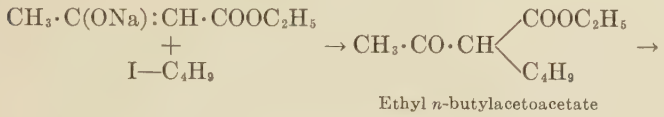
$$\begin{array}{c} CH_3 \cdot C(ONa) : CH \cdot COOC_2H_5 \\ + \\ I - C_8H_{17} \end{array} \rightarrow \begin{array}{c} CH_3 \cdot CO \cdot CH \cdot COOC_2H_5 \\ | \\ C_8H_{17} \end{array}.$$

By the ketone decomposition it yields methylnonylketone,

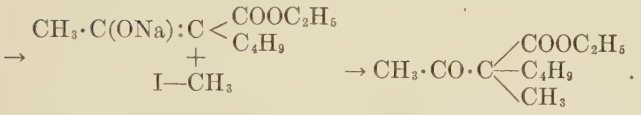
$$CH_3 \cdot CO \cdot CH_2 \cdot C_8H_{17}.$$

By the acid decomposition ethyl *n*-octylacetoacetate gives capric acid, $C_{10}H_{20}O_2$, indicating the presence in this acid of a normal carbon chain (137),

2. Heptylic acid is obtainable from lævulose by the cyanohydrin-synthesis (**209**), but can be built up synthetically from ethyl acetoacetate by the successive introduction of a methyl-group and a *n*-butyl-group, a reaction proving it to be *methyl*-n-*butylacetic acid:*

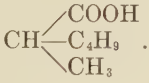


Ethyl *n*-butylacetoacetate



Ethyl methyl-*n*-butylacetoacetate

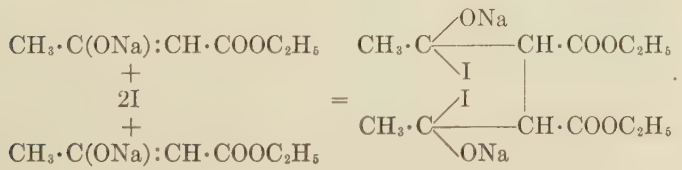
By the acid decomposition ethyl methyl-*n*-butylacetoacetate yields methyl-*n*-butylacetic or hexanecarboxylic-2 acid,



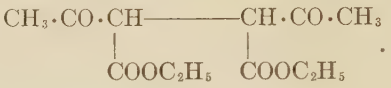
3. 3-Ketonic acids are obtained by the action of ethyl acetoacetate on the esters of the 1-halogen-substituted fatty acids, followed by the ketone decomposition:

By the ketone decomposition this derivative gives

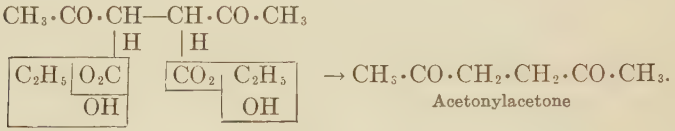
4. The action of iodine on ethyl sodioacetoacetate unites two molecules:



Elimination of two molecules of sodium iodide converts this compound into *diethyl diacetylsuccinate*,



Boiling diethyl diacetylsuccinate with a twenty per cent. solution of potassium carbonate yields carbon dioxide, ethyl alcohol, and *acetonylacetone* (200):



Butanone-2-carboxylic-1 or Lævulic Acid, $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot COOH$.

234. *Lævulic acid* is the simplest 3-ketonic acid. It can be obtained from ethyl acetoacetate by the action of ethyl monochloroacetate in accordance with the synthetic method described in 233, 3, the symbol R in the formula representing one atom of hydrogen. When hexoses are boiled with concentrated hydrochloric acid, lævulic acid is produced (210). Usually it is prepared by this method, although hitherto its mechanism has not been explained fully.

Lævulic acid is crystalline, melts at 33·5°, and boils with slight decomposition at 250°. It exhibits all the reactions characteristic of ketones, yielding an oxime and a hydrazone, and an addition-product with hydrogen cyanide.

Mesoxalic Acid, $C_3H_2O_5,H_2O$.

Mesoxalic acid is a type of the *dibasic ketonic acids*. Its constitution is proved through the formation of *ethyl mesoxalate* by boiling diethyl dibromomalonate, $Br_2C(COOC_2H_5)_2$, with barium-hydroxide solution:

$$(C_2H_5OOC)_2C\boxed{Br_2+Ba}(OH)_2=(C_2H_5OOC)_2C(OH)_2+BaBr_2.$$

Mesoxalic acid is an important decomposition-product of uric acid. Like glyoxylic acid (230), it can be obtained only with one molecule of water; although an ester of the anhydrous acid is known, and adds water very readily. In consequence, the constitution $(COOH)_2C(OH)_2$ must be assigned to the free acid (149). It has most of the properties of ketones, just as chloral hydrate (201) and glyoxylic acid display

most of the reactions of aldehydes. Boiling mesoxalic acid with water eliminates carbon dioxide and forms glyoxylic acid:

$$\overline{CO_2}\,H\cdot C(OH)_2\cdot COOH.$$

Such a decomposition of a compound containing a carbon atom loaded with four negative groups should occasion no surprise. The corresponding change is effected less readily with malonic acid, for it does not lose carbon dioxide until heated above its melting-point, a temperature between 140° and 150°.

TAUTOMERISM.

235. The conversion of ethyl acetoacetate into its sodium derivative, and the interaction of this substance with an alkyl iodide, yield derivatives with the introduced alkyl-group undoubtedly in union with a carbon atom (**232**). Sometimes the reaction proceeds differently, the metallic atom of the sodium derivative being replaced by a substituent attached to the molecule through oxygen. An example is furnished by the interaction of ethyl sodiocetoacetate and ethyl chlorocarbonate (**263**), two compounds being formed. The one produced in smaller proportion is the carbon derivative:

$$\begin{aligned} &\begin{matrix} ONa \\ | \\ CH_3\cdot C{:}CH\cdot COOC_2H_5 \\ | \\ Cl\cdot COOC_2H_5 \end{matrix} \rightarrow \begin{matrix} ONa \\ | \\ CH_3\cdot C{-}{-}CH\cdot COOC_2H_5 = \\ | \quad | \\ Cl \quad COOC_2H_5 \end{matrix} \\ &= CH_3\cdot CO\cdot \begin{matrix} COOC_2H_5 \\ | \\ CH \\ | \\ COOC_2H_5 \end{matrix} + NaCl. \end{aligned}$$

The identity of this product with that formed by the interaction of acetyl chloride and diethyl sodiomalonate proves its constitution:

$$CH_3\cdot CO\boxed{Cl+Na}\cdot CH(COOC_2H_5)_2 \rightarrow CH_3\cdot CO\cdot CH(COOC_2H_5)_2.$$

The main product is an isomeride, the oxygen derivative:

$$\begin{matrix} CH_3\cdot C(ONa){:}CH\cdot COOC_2H_5 \\ + \\ Cl{-}COOC_2H_5 \end{matrix} = \begin{matrix} CH_3\cdot C{:}CH\cdot COOC_2H_5 \\ | \\ O\cdot COOC_2H_5 \end{matrix} + NaCl.$$

The presence of a double carbon bond in the molecule is proved by the instantaneous formation of an addition-product with bromine.

The mechanism of the interaction of ethyl chlorocarbonate and sodioacetylacetone is exactly analogous, the carbon derivative being produced in small proportion:

$$\begin{array}{l} CH_3\cdot C(ONa):CH\cdot CO\cdot CH_3 \\ \qquad\qquad + \\ Cl{-}COOC_2H_5 \end{array} \rightarrow \begin{array}{l} CH_3\cdot CO\cdot CH\cdot CO\cdot CH_3 \\ \qquad\quad | \\ \qquad COOC_2H_5 \end{array}.$$

The constitution of this compound follows from its ready decomposition into potassium acetate and ethyl acetoacetate by heating with an equimolecular proportion of potassium hydroxide:

$$\begin{array}{l} \qquad\quad H\cdot \mid OK \\ \qquad\quad + \\ CH_3\cdot CO\cdot CH\cdot \mid CO\cdot CH_3 \\ \qquad\quad | \\ \qquad COOC_2H_5 \end{array} = \underset{\text{Ethyl acetoacetate}}{CH_3\cdot CO\cdot CH_2\cdot COOC_2H_5} + \underset{\substack{\text{Potassium}\\ \text{acetate}}}{CH_3\cdot COOK}.$$

The oxygen derivative, however, is the principal product:

$$\begin{array}{l} CH_3\cdot C(ONa):CH\cdot CO\cdot CH_3 \\ \qquad\qquad + \\ Cl{-}COOC_2H_5 \end{array} = \begin{array}{l} CH_3\cdot C:CH\cdot CO\cdot CH_3 \\ \qquad\quad | \\ \qquad O\cdot COOC_2H_5 \end{array} + NaCl.$$

Its formula is proved by the ready formation of an addition-product with bromine, and its decomposition into acetylacetone, ethyl alcohol, and carbon dioxide by dilute alkalis at the ordinary temperature:

$$\begin{array}{l} CH_3\cdot C:CH\cdot CO\cdot CH_3 \\ \qquad\quad | \\ \qquad O\cdot \boxed{CO_2\ C_2H_5} \\ \qquad\quad + \quad | \\ \qquad H{-}\!\!-\!\!-\boxed{\ OH} \end{array} = \underset{\text{Acetylacetone}}{CH_3\cdot C(OH):CH\cdot CO\cdot CH_3} + C_2H_5\cdot OH + CO_2.$$

The interaction of ethyl acetoacetate and acid chlorides can be controlled so as to produce either a carbon derivative or an oxygen derivative. By the usual method of preparing ethyl sodioacetoacetate first, and then bringing it into contact with the acid chloride, a carbon derivative is produced. In contrast, slow addition of the acid chloride to a solution of ethyl acetoacetate in pyridine (387) gives only the oxygen derivative:

$$\begin{array}{l} CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \\ \qquad\quad | \\ \qquad CO\cdot CH_3 \end{array} ; \quad \begin{array}{l} CH_3\cdot C{=}CH\cdot COOC_2H_5 \\ \qquad\quad | \\ \qquad O\cdot CO\cdot CH_3 \end{array}.$$

Carbon derivative (Does not give an addition-product with bromine)

Oxygen derivative (Gives an addition-product with bromine)

Similar equivocal reactions have been observed for many compounds with the grouping —CO·CH_2·CO—. Formerly the production of a carbon derivative was believed to be occasioned by direct attachment of the sodium atom to carbon, —CO·CHNa·CO—, and that of the oxygen derivative by direct union of the sodium atom with oxygen, —C(ONa):CH·CO—. Accordingly, compounds of this type were assumed to undergo continual alternation between the groupings —CO·CH_2·CO— and —C(OH):CH·CO—. The phenomenon received the name *tautomerism* or *desmotropy*.

Although later investigation detailed in the sequel proved the metallic atom in the sodium compounds to be in union with oxygen, it also demonstrated the liquid derivatives such as ethyl acetoacetate to be a mixture of two isomerides of the type indicated, each being transformed very readily into the isomeric compound. This view is based on the direct isolation of the tautomeric forms.

Ethyl acetoacetate is the classic example of a tautomeric substance. By cooling it to a low temperature, Knorr isolated the *ketonic form*, CH_3·CO·CH_2·$COOC_2H_5$, in crystals melting at −39°. By the action of an equivalent quantity of anhydrous hydrogen chloride on a suspension of ethyl sodioacetoacetate in well-cooled light petroleum, followed by filtration of the sodium chloride and evaporation of the solvent at a low temperature, Knorr isolated the *enolic form*

$$CH_3 \cdot C(OH):CH \cdot COOC_2H_5,$$

a substance requiring for solidification the refrigerating action of liquid air. This separation proves the sodium derivative to have the enolic structure.

More recently it has been found possible to separate the two tautomerides by fractional distillation *in vacuo*, a quartz flask being employed to obviate enolization arising through the influence of the alkali present in glass.

236. The ketonic form and the enolic form of a tautomeric substance admit of ready identification by both physical and chemical means. The most important physical method is furnished by refraction, the presence of a double carbon bond in the enolic form and its absence from the ketonic form making the refraction of the enolic compound higher than that of the ketonic compound (120). By the aid of this physical property, the proportion of the two isomerides present in a liquid mixture can be determined, provided the refraction of each component in the pure state is known.

Two main chemical methods of distinguishing the two forms are available:

1. Addition of a small proportion of ferric chloride to a dilute aqueous or alcoholic solution of an enolic compound produces a deep coloration, usually violet; but ketonic derivatives remain colourless.

2. The action of bromine on an alcoholic solution, KURT H. MEYER having discovered that in this solution enolic compounds form addition-products with bromine instantaneously, but that ketonic compounds do not. The method was applied by him to determine the proportion of the enolic form present in a tautomeric mixture.

The introduction of alkyl-groups into diethyl malonate also being effected by means of the sodium derivative, it is reasonable to anticipate complete analogy between the mechanism of that reaction and that characteristic of ethyl acetoacetate. The bromine-method affords confirmation of the accuracy of this assumption, and indicates diethyl monosodiomalonate to have the tautomeric formula

$$C_2H_5OOC\cdot CH{:}C{<}\begin{matrix}ONa\\OC_2H_5\end{matrix}.$$

Interaction of this substance and an alkyl halide first yields an addition-product of the formula

$$C_2H_5OOC\cdot \underset{\displaystyle R}{\overset{\displaystyle |}{CH}}\cdot C{<}\begin{matrix}ONa\\X\\OC_2H_5\end{matrix},$$

X representing a halogen atom, and R an alkyl-radical. Elimination of sodium halide from this compound produces the diethyl alkylmalonate.

These aids can be applied to the elucidation of the conditions governing the *ketonization* of an enolic compound, and the inverse *enolization* of a ketonic compound. The nature of the solvent is of primary importance. For ethyl acetoacetate in the liquid state the equilibrium between the two forms corresponds with a small percentage of the enolic derivative, and about 90 per cent. of the ketonic form. The subjoined table indicates the percentage of the enolic form of ethyl acetoacetate in various solvents at 18°, the amounts being determined by titration with bromine.

Solvent.	Percentage of Enolic Form.	Solvent.	Percentage of Enolic Form.
Methyl alcohol	6·9	Methyl alcohol (50 per cent)	1·5
Ethyl alcohol	12·0	Ether	27·1
Amyl alcohol	15·3	Carbon disulphide	32·4
Water	0·4	Hexane	46·4

For liquid ethyl acetoacetate the temperature has little influence on the equilibrium, but the freshly-distilled product contains between 20 and 25 per cent. of the enolic form, and becomes transformed slowly into the ketonic modification. There are other instances of rise of temperature causing displacement of the equilibrium towards the enolic side, although usually not to any great extent.

The velocity of translation of each form can be determined by starting with the pure modifications, and noting the proportion of each component present after the lapse of known intervals of time. The velocity-constant of the ketonization of ethyl acetoacetate has been proved to be much greater than that of the enolization. Different tautomeric compounds generally exhibit wide divergence in the velocity of transformation in either direction.

A qualitative demonstration of the transformation of the enolic form of ethyl acetoacetate into the ketonic modification can be made by adding an equivalent amount of hydrogen chloride to a dilute aqueous solution of ethyl sodioacetoacetate. The enolic form separates in fine drops, its solubility in water at 0° being about 0·5 per cent. Owing to transformation of the enolic form into the ketonic modification, the drops gradually dissolve, the solubility of the ketonic derivative in water at 0° being about 11 per cent.

Enolic compounds dissolve instantly in caustic alkali; but ketonic compounds do not, their solution proceeding slowly as they change to the enolic form. On subsequent addition of acid, initially the enolic modification is obtained, but not the ketonic component.

Tautomerism of Oximes.

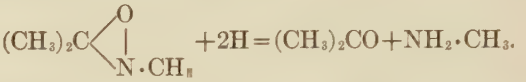
237. The structural formula, $\begin{matrix}R\\R'\end{matrix}\!>\!C{=}{=}NOH$, has been assigned to the oximes (**103**). The action of hydroxylamine on aldehydes and ketones admits of another explanation, indicated in the scheme

$$>CO+\begin{matrix}HO\\H\end{matrix}\!\!>\!NH=H_2O+>C\!\!<\!\!\begin{matrix}O\\|\\NH\end{matrix}.$$

Experiments directed to identifying the correct formula have proved the oximes to be tautomeric in the sense of the scheme

$$>C{=}{=}NOH \rightleftarrows >C\!\!<\!\!\begin{matrix}O\\|\\NH\end{matrix}.$$

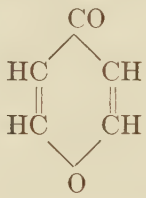
The following procedure exemplifies the method. During the interaction of acetoxime and methyl iodide, the methyl-group unites with nitrogen, as is proved by reduction of the product to methylamine and acetone:



Addition of sodium methoxide to a mixture of methyl iodide and the oxime is attended by the preliminary formation of the sodium derivative of the ketoxime, and later by production of an isomeric substance convertible by hydrogen chloride into acetone and a compound, $NH_2 \cdot OCH_3$. Heating with hydrogen iodide transforms this derivative into hydroxylamine and methyl iodide, proving its methyl-group to be in union with oxygen.

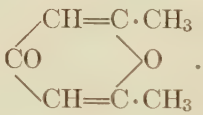
PYRONE DERIVATIVES.

238. Certain compounds assumed to contain the group

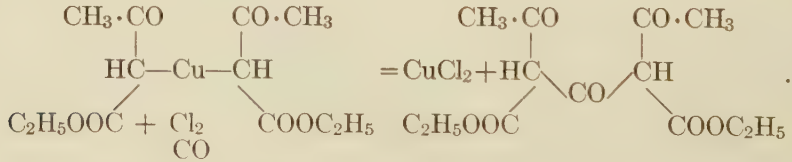


are known. They are termed *pyrone derivatives*, and some of them are natural products.

An important pyrone derivative is *dimethylpyrone*:

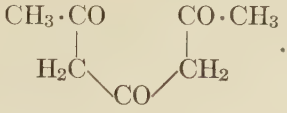


It can be synthesized from ethyl copper-acetoacetate and carbonyl chloride (**263**):

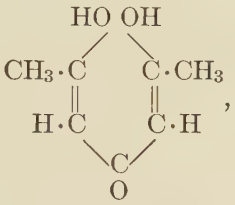


Saponification with dilute sulphuric acid eliminates two molecules of car-

bon dioxide from the molecule simultaneously, and should yield a compound of the formula

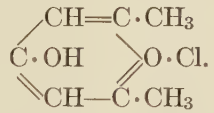


The tautomeride,

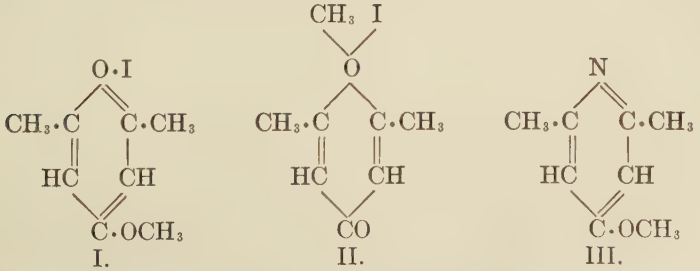


however, is formed, and loses one molecule of water with production of dimethylpyrone.

239. Dimethylpyrone is characterized by its ability to form with acids addition-products of the type of salts. These "salts" are formed by dissolving dimethylpyrone in an aqueous solution of hydrogen chloride, oxalic acid, etc., and are obtained in a crystalline form by the spontaneous evaporation of the solutions. By dissolving them in a large proportion of water, they are hydrolyzed completely. COLLIE and TICKLE, the discoverers of these compounds, assume the *quadrivalency of the oxygen atom* closing the carbon chain, thus attributing to *dimethylpyrone hydrochloride* the structure



This mode of expressing the constitution of dimethylpyrone has been adopted instead of the earlier formula $COC_4H_2(CH_3)_2{>}O{<}\begin{matrix}H\\Cl\end{matrix}$, VON BAEYER having proved the addition-product of dimethylpyrone with methyl iodide to have formula I, and not formula II, his proof being based on the conversion of the addition-product by the action of ammonia into *methoxylutidine* (**389**), formulated in III:



On account of their analogy to the ammonium salts these compounds have been named *oxonium salts*. They are to be regarded as true salts or electrolytes, because they possess all the properties characteristic of the salts formed by weak bases with strong acids, their aqueous solutions being strongly acidic in reaction in consequence of extensive hydrolytic dissociation, their electric conductivities in solution being almost equal to those of the free acid, and so on.

The power of forming oxonium salts does not seem to be limited to dimethylpyrone and analogous compounds. VON BAEYER and VILLIGER have demonstrated the ability of oxygen-containing compounds belonging to various classes of organic bodies, such as alcohols, aldehydes, esters, and other substances, to yield crystalline derivatives with complex acids, such as hydroferrocyanic acid. It is possible, though not fully established, that these substances are oxonium salts.

WILLSTÄTTER proved the *anthocyanins*, the colouring principles of many plants, to be oxonium salts (346).

AMINO-ACIDS.

240. The *amino-acids* contain one or more amino-groups in direct union with carbon. They are of physiological importance, many being decomposition-products of proteins, and some being natural products. They are synthesized by several methods.

1. By the action of the halogen-substituted fatty acids on ammonia, a method analogous to the formation of amines:

$$H_2N\boxed{H+Cl}H_2C\cdot COOH = H_2N\cdot CH_2\cdot COOH + HCl.$$

2. By the reduction of oximes with sodium amalgam:

$$R\cdot C(NOH)\cdot COOH + 4H = R\cdot CHNH_2\cdot COOH + H_2O.$$

This reaction furnishes a method of converting ketonic acids into amino-acids.

3. 1-Amino-acids are formed by the action of ammonia on the cyanohydrins of aldehydes or ketones, and subsequent hydrolysis of the cyano-group (STRECKER):

$$\underset{\text{Acetaldehyde}}{CH_3\cdot C\begin{cases}H\\O\end{cases}} \rightarrow \underset{\text{Lactonitrile}}{CH_3\cdot C\begin{cases}H\\OH\\CN\end{cases}};\quad +NH_3, \rightarrow$$

$$\rightarrow \underset{\text{Alanine nitrile}}{CH_3\cdot C\begin{cases}H\\NH_2\\CN\end{cases}} \rightarrow \underset{\text{Alanine}}{CH_3\cdot C\begin{cases}H\\NH_2\\COOH\end{cases}}.$$

Most of the amino-acids crystallize well, and dissolve readily in water; but they are either insoluble or only slightly soluble in alcohol or ether. Many of the 1-amino-acids have a sweet taste, but the dibasic acids are sour. Most of these acids have a high melting-point in the neighbourhood of 200°, a phenomenon perhaps explicable by the formation of inner salts corresponding with the formula (compare betaine, **242**)

$$\begin{array}{l} R\cdot CH\text{—}CO \\ \quad\;\; | \qquad\;\; | \\ \quad NH_3\text{—}O \end{array} \quad \text{instead of} \quad \begin{array}{l} R\cdot C\cdot COOH \\ \quad\;\; | \\ \quad NH_2 \end{array}.$$

Their copper salts are noteworthy, and are prepared by boiling aqueous solutions of the acids with copper carbonate. As they are not

readily soluble, these salts separate from their cooled solutions in beautiful crystals with an intense blue colour. In aqueous solution they are not characterized by the possession of all the properties of copper ions. This fact and their dark-violet colour indicate their copper to be in complex union. Aqueous solutions of many amino-acids give with ferric chloride an intense red coloration.

The amino-acids possess two opposed characteristics, for they form salts with both bases and acids, and are therefore both basic and acidic simultaneously.

Replacement of the hydrogen of the amino-group by radicals yields amino-acids of a more complex character, exemplified by their yielding with acid chlorides an acid amide having one hydrogen atom of the amino-group replaced, a reaction recalling the behaviour of ammonia:

$$R\cdot CO\boxed{Cl+H}HN\cdot CH_2\cdot COOH = R\cdot CO\cdot NH\cdot CH_2\cdot COOH + HCl.$$

Compounds of this kind are therefore both amino-acids and acid amides.

Amino-acids with the hydrogen of the amino-group replaced by alkyl-groups are known also. They are obtained by the action of amines, instead of ammonia, on the halogen-substituted acids:

$$(CH_3)_2N\boxed{H+Cl}H_2C\cdot COOH = (CH_3)_2N\cdot CH_2\cdot COOH + HCl.$$

The amino-acids undergo most of the decompositions characteristic of amines, giving with nitrous acid hydroxy-acids, just as the amines yield alcohols.

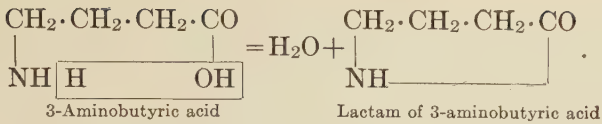
241. Like those of the halogen-substituted acids and hydroxy-acids (**176** and **180**), the properties of the amino-acids depend on the position of the characteristic amino-group relative to the carboxyl-group. The 1-amino-acids readily yield anhydrides (acid amides) by the elimination of two molecules of water from two molecules of acid:

$$\begin{array}{l} CH_2\cdot NH\boxed{H\ HO}OC \\ | \qquad\qquad\qquad\quad | \\ CO\boxed{OH\qquad H}HNCH_2 \end{array} = 2H_2O + \begin{array}{l} CH_2NH\cdot OC \\ | \qquad\qquad | \\ CO\text{——}HNCH_2. \end{array}$$

The 2-amino-acids easily lose ammonia, with formation of unsaturated acids, 2-aminopropionic acid, obtained from 2-iodopropionic acid, being converted by heat into acrylic acid and ammonia:

$$\boxed{NH_2}\cdot CH_2\cdot CH\boxed{H}\cdot COOH = NH_3 + CH_2{:}CH\cdot COOH.$$

Like the 3-hydroxy-acids, the 3-amino-acids yield inner anhydrides. On account of their similarity to the lactones, these substances are termed *lactams:*

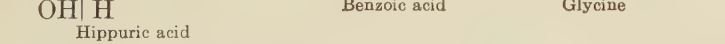


3-Aminobutyric acid — Lactam of 3-aminobutyric acid

Emil Fischer demonstrated the possibility of obtaining the *esters of amino-acids* by the ordinary method, dissolving the acids in absolute alcohol and passing gaseous hydrogen chloride into this solution (91). Hydrochlorides are the primary products, the amino-group in these esters retaining its basic character, as is exemplified by the *ethyl ester of glycine hydrochloride*, $C_2H_5OOC \cdot CH_2 \cdot NH_2,HCl$. The esters are prepared by the action of concentrated potassium hydroxide at a low temperature on aqueous solutions of the hydrochlorides, and immediate extraction with ether. Emil Fischer found these esters well adapted for the purification and separation of amino-acids, for they can be distilled in a high vacuum. This fact is of great importance in the chemistry of proteins, these substances being resolved into a mixture of such acids by the action of acids or bases.

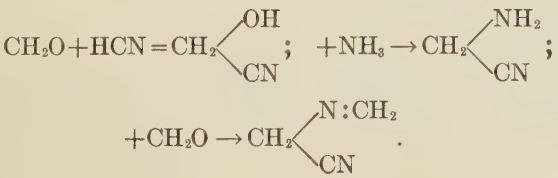
Individual Members.

242. *Glycine* (glycocoll or aminoacetic acid), $NH_2 \cdot CH_2 \cdot COOH$, can be obtained by boiling glue with dilute sulphuric acid or with barium hydroxide. It owes the name "glycocoll" to this method of formation and to its sweet taste (γλυκύς, sweet; κόλλα, glue). It is prepared also from *hippuric acid*, a constituent of the urine of horses. Hippuric acid is glycine with one hydrogen atom of the amino-group replaced by benzoyl, C_6H_5CO, and it has the formula $C_6H_5 \cdot CO \cdot NH \cdot CH_2 \cdot COOH$. Like all acid amides, it is decomposed by boiling with dilute acids, with addition of the elements of water:

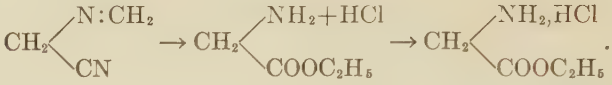


Hippuric acid — Benzoic acid — Glycine

A method well adapted for the preparation of glycine and its derivatives depends on the interaction of formaldehyde, ammonium chloride, and potassium cyanide in well-cooled aqueous solution. *Methyleneamino-acetonitrile*, $CH_2:N \cdot CH_2 \cdot CN$, crystallizes, being formed in accordance with the scheme



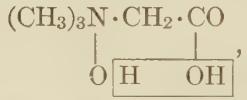
On boiling the carbonitrile with an alcoholic solution of hydrogen chloride, the cyano-group is exchanged for $—COOC_2H_5$, and the methene-group of $—N:CH_2$ becomes replaced by two atoms of hydrogen, with production of the hydrochloride of the ethyl ester of glycine:



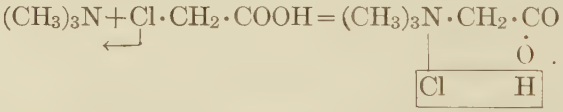
Glycine is a crystalline solid, and melts at 232° with decomposition. It is soluble in water very readily, and is insoluble in absolute alcohol. Like many amino-acids, it forms a well-crystallized blue copper salt, soluble with difficulty in water, and obtained by boiling copper carbonate with a solution of glycine. This derivative crystallizes with one molecule of water of crystallization, and has the formula

$$(NH_2 \cdot CH_2 \cdot COO)_2Cu,H_2O.$$

Betaine, $C_5H_{11}O_2N$, is a derivative of trimethylglycine. It is a constituent of the juice of the sugar-beet, and accumulates in the molasses during the manufacture of sugar. It is an inner ammonium salt,



being obtained synthetically from trimethylamine by the action of monochloroacetic acid, with elimination of hydrogen chloride:



This process is analogous to the interaction of alkyl halides and tertiary amines to form the salts of quaternary ammonium bases (63).

Betaine yields large crystals with one molecule of water, expelled at 100°, or absorbed in a sulphuric-acid desiccator. Heating decomposes betaine, with formation of trimethylamine.

Many tertiary amines can be converted into substances with the constitution of inner salts of ammonium bases, and analogous to that of betaine. These compounds are designated *betaines*.

Alanine, or 1-aminopropionic acid, $CH_3 \cdot CH(NH_2) \cdot COOH$, is prepared synthetically by the action of ammonia on 1-chloropropionic acid.

Leucine, or 1-amino*iso*butylacetic acid,

$$(CH_3)_2CH\cdot CH_2\cdot CH(NH_2)\cdot COOH,$$

accompanies glycine as a product of the decomposition of proteins by the action of acids or alkalis, or by putrefaction. It is obtained synthetically from *iso*valeraldehydeammonia by the action of hydrogen cyanide, and hydrolysis of the carbonitrile:

$$(CH_3)_2CH\cdot CH_2\cdot C\begin{matrix}H\\ \boxed{OH+H}\\ NH_2\end{matrix}CN \rightarrow$$

*iso*Valeraldehydeammonia

$$\rightarrow (CH_3)_2CH\cdot CH_2\cdot CH(NH_2)\cdot CO_2H.$$

Leucine

iso*Leucine*, or 1-amino-2-methylvaleric acid,

$$\begin{matrix}CH_3\\ C_2H_5\end{matrix}>CH\cdot CH(NH_2)\cdot COOH,$$

is also a decomposition-product of proteins. Its constitution is proved by synthesis. The aldehyde formed by oxidation of the optically active amyl alcohol secondary butylcarbinol yields by the method of **240**, 3, an amino-acid identical with *iso*leucine.

Fusel-oil is a by-product in alcoholic fermentation (**43**). Ehrlich proved it not to be derived from the sugars, but from leucine and *iso*leucine formed by decomposition of the proteins present in the fermenting liquid. These proteins are constituents of the grain, potatoes, and other material employed in the manufacture of alcohol. Fermentation of sugar with a pure yeast-culture in presence of leucine forms *iso*butylcarbinol as a by-product; with *iso*leucine it gives secondary butylcarbinol. These two amyl alcohols are the principal constituents of fusel-oil (**47**).

The general equation representing the mechanism of the decomposition of amino-acids by yeast, or their alcoholic fermentation, is

$$R\cdot CH(NH_2)\cdot COOH+H_2O=R\cdot CH_2OH+CO_2+NH_3.$$

The leucine obtained from proteins is optically active. Its formula contains an asymmetric carbon atom.

243. *Asparagine* is present often in sprouting seeds, between 20 and 30 per cent. in dried lupine-seeds. It is *aminosuccinamic acid*, $C_2H_3(NH_2)<\begin{matrix}CONH_2\\ COOH\end{matrix}$, for hydrolysis converts it into *aminosuccinic*

acid (*aspartic acid*), $COOH \cdot CH(NH_2) \cdot CH_2 \cdot COOH$. The structure of this derivative is inferred from its conversion into malic acid by the action of nitrous acid. Asparagine prepared from seeds is sometimes dextrorotatory, but is generally lævorotatory. The dextro-form is sweet, but the lævo-modification is tasteless.

Glutamine or *glutamic acid* is a constituent of the seeds of sprouting plants, and is homologous with asparagine. It is the amic acid (**163**) of 1-aminoglutaric acid, $COOH \cdot CH(NH_2) \cdot CH_2 \cdot CH_2 \cdot COOH$.

In addition to the monoamino-acids, diamino-acids also are obtained by decomposing proteins with acids. Some of them merit description.

Lysine, $C_6H_{14}O_2N_2$, is decomposed by putrefaction-bacilli with formation of 1:5-diaminopentane (**159**). It has the formula

$$NH_2 \cdot CH_2 \cdot (CH_2)_3 \cdot CH < \begin{matrix} NH_2 \\ COOH \end{matrix},$$

and is 1:5-diaminopentanecarboxylic-1 acid.

By synthesis Emil Fischer proved this formula to be correct. On bringing ethyl monosodiomalonate into contact with 3-chlorobutyronitrile, *ethyl 3-cyanopropylmalonate* is formed:

$$\underset{\text{Ethyl monosodiomalonate}}{(COOC_2H_5)_2CHNa} + \underset{\text{3-Chlorobutyronitrile}}{Cl \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CN} \rightarrow$$

$$\rightarrow \underset{\text{Ethyl 3-cyanopropylmalonate}}{(COOC_2H_5)_2CH \cdot (CH_2)_3 \cdot CN} .$$

Ethyl nitrite and sodium ethoxide convert this ester by elimination of a carbethoxyl-group into the sodium salt of an oxime:

$$NC \cdot (CH_2)_3 \cdot CH \begin{matrix} COOC_2H_5 \\ COOC_2H_5 \end{matrix} \rightarrow \underset{\text{Oxime}}{NC \cdot (CH_2)_3 \cdot C \begin{matrix} NOH \\ COOC_2H_5 \end{matrix}} .$$

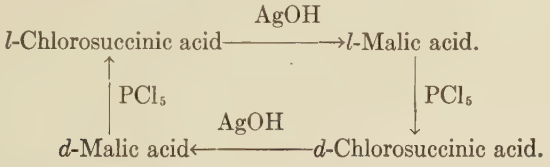
Reduction of this oxime with sodium and alcohol converts the NOH-group into an amino-radical, and the cyano-group into CH_2NH_2, with formation of inactive lysine, $CH_2NH_2 \cdot (CH_2)_3 \cdot CH < \begin{matrix} NH_2 \\ COOH \end{matrix}$.

Ornithine is the next lower homologue of lysine, and has the formula $C_5H_{12}O_2N_2$ or $NH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot COOH$. Bacteria convert it into 1:4-diaminobutane (**159**). Its structure is proved by Emil Fischer's synthesis (**349**).

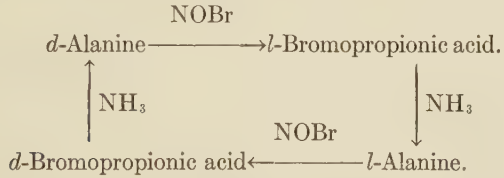
THE WALDEN INVERSION AND THE MODE OF LINKING OF ATOMS.

244. When one group attached to an asymmetric carbon atom is replaced by another, it is impossible to predict the sign of the rotation of the new compound, it being sometimes the same as that of the original substance, and sometimes opposite to it. By a series of substitutions, Walden transformed an optically active compound into its optical anti-

pode. *l*-Chlorosuccinic acid was converted by the action of moist silver oxide into *l*-malic acid, and this substance was transformed by means of phosphorus pentachloride into *d*-chlorosuccinic acid. On the other hand, starting from *d*-chlorosuccinic acid, a similar operation yielded *l*-chlorosuccinic acid. These changes are indicated in the cyclic scheme



The following is another reaction-cycle, worked out by Emil Fischer:



Here the transposition probably accompanied the replacement of the amino-group by bromine under the influence of nitrosyl bromide, and was not due to the action of ammonia, for with widely differing experimental conditions the same product with a similar sign of rotation invariably was produced in the operation. Although *d*-alanine reacted with nitrosyl bromide to form *l*-bromopropionic acid, under identical conditions its ester yielded *d*-bromopropionic acid.

Senter discovered many other examples of the Walden inversion, and demonstrated the complex nature of the phenomenon.

The conversion of an optically active compound into its optical isomeride necessitates an interchange of position between two of the groups or atoms attached to the asymmetric carbon atom. For example, in Fig. 64 the transformation of I into II only requires *B* and

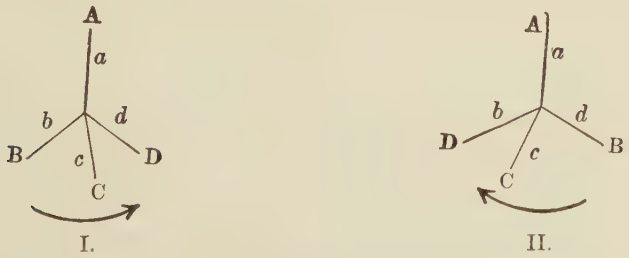
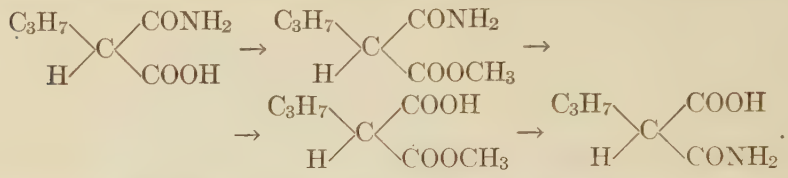


Fig. 64.—Conversion of an Optically Active Substance into its Optical Isomeride.

D to exchange positions. An experimental demonstration of this fact has been attained by the series of changes indicated in the scheme



Although there was no alteration of position, the group $CONH_2$ was transformed into COOH, and COOH into $CONH_2$. The rotation of the initial product proved to be opposite in sign to that of the final product.

In WALDEN's inversion or in a racemisation there must be a true exchange of position between two groups. In accordance with the views of atomic linking hitherto accepted, this process could be possible only through a momentary severance of the two groups from the asymmetric carbon atom, followed by a reunion at the reverse positions. The transformation of maleic acid into fumaric acid and its reversal (171) also would involve either a momentary rupture of the double bond, followed by reunion of the residues at the reverse positions; or an exchange of position between hydrogen and carboxyl would be necessary.

There is one very important objection to the acceptance of this view. Almost all reactions of this type are quantitative, a result not to be anticipated in a process involving the molecular disintegration attendant on the scission of two groups from one carbon atom.

The modern view of atomic structure has eliminated this difficulty.

RUTHERFORD and BOHR regard the atom as consisting of a positively-charged nucleus surrounded by negative electrons, and having a radius of the order of 10^{-12} cm. These electrons move in concentric rings, or possibly in ellipses, the radius of the outermost ring of electrons being about 10^{-8} cm. ("Inorganic Chemistry," 277). The number of electrons on the outermost ring is equal to the valency of the atom, that for carbon being four. This relation has gained for them the name *valency-electrons*.

A single bond between two atoms is originated by the severance of an electron from each atom, these electrons describing a circular path in a plane at right angles to the line uniting the nuclei. The centre of the circle is the point of intersection of this line and the plane, the line being therefore the axis of the circle. For a carbon atom in union with four atoms or groups the existence of four such electron-paths around the nucleus carrying the other electrons must be assumed.

The theory thus outlined does not demand a rupture of the bonds during an exchange of position by two groups, but only requires a simple transposition on the surface of the sphere of the valency-electrons and the attached atoms. It affords an explanation of the quantitative nature both of racemisation and of the conversion of a doubly-linked *cis*-form into the corresponding *trans*-modification.

This hypothesis also serves to explain the WALDEN inversion. The interaction of *d*-bromopropionic acid (I) and silver hydroxide can follow two different courses. One of them involves direct action on the bromine atom, and its replacement by the hydroxyl-group. The lactic acid formed has the same configuration as the bromopropionic acid, and there has been no inversion. Substitution of bromine for the hydroxyl-group by the aid of phosphorus pentabromide or another reagent regenerates the original acid.

In the other type of reaction, the molecule of silver hydroxide attacks that of the bromopropionic acid as indicated in I, the valency-electron of the silver atom penetrating between methyl, hydrogen, and carboxyl. After fission of the silver bromide, the repulsion exerted by the valency-electron of the hydroxyl-group on the valency-electrons of the other three groups compels them to assume the positions indicated in II. On replacing the hydroxyl-group by bromine by the aid of phosphorus pentabromide or another reagent, a substance of formula III is obtained. It is the optical antipode of I, as can be proved by rotating III through 180°, the configuration produced being represented by IV. In this instance a WALDEN inversion has taken place (Fig. 65):

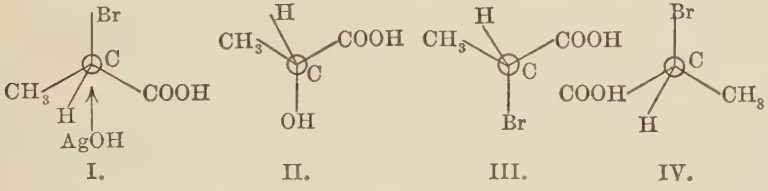


FIG. 65.—WALDEN'S Inversion.

The tetrahedral grouping round the carbon atom follows from this hypothesis, the positively-charged nuclei of the four atoms in union with the carbon atom repelling each other, but being maintained in their circular orbits by the attraction of the nucleus. The tendency of these electrons must be to take up positions as far apart as possible. Location of them at the angles of a regular tetrahedron with its centre coincident with that of the nucleus of the central carbon atom fulfils this condition.

The strain-theory of VON BAEYER (120) possibly is explicable also by the mutual repulsion exerted by the electrons.

ETHYL DIAZOACETATE.

245. CURTIUS obtained a yellow oil of characteristic odour by the action of nitrous acid on the ethyl ester of glycine. This substance has the formula $C_4H_6O_2N_2$, and is exploded by heat. The method of its formation is indicated in the equation

$$\underset{\text{Glycine ethyl ester}}{C_2H_5OOC\cdot CH_2\cdot NH_2} + HNO_2 = C_2H_5OOC\cdot CH\begin{matrix}N\\ \|\\ N\end{matrix} + 2H_2O.$$

It is *ethyl diazoacetate*, and also is termed *diazoacetic ester*.

The structural formula indicated is proved to be correct by numerous transformations. They can be classified in three divisions.

I. The first group includes the reactions involving the elimination of the diazo-nitrogen. As an example may be cited the conversion of ethyl diazoacetate into ethyl glycollate by the aid of dilute acids:

$$C_2H_5OOC\cdot CH\begin{matrix}\boxed{N}\\ \|\\ N\end{matrix} + \overset{H}{\dot{O}}H = C_2H_5OOC\cdot CH\begin{matrix}H\\ OH\end{matrix} + N_2.$$

BREDIG discovered this reaction to be accelerated greatly by the catalytic agency of hydrogen ions, and on this observation he based one of the best methods for the detection and quantitative estimation of such ions.

Concentrated hydrochloric acid yields analogously ethyl monochloroacetate, and iodine ethyl di-iodoacetate. Organic acids produce acidylglycollic acid esters:

$$CH_3\cdot COO\overset{H}{\dot{}} + \begin{matrix}N\\ \|\\ N\end{matrix}\!\!>CH\cdot COOC_2H_5 = CH_3\cdot COO\begin{matrix}H\\ >\end{matrix}CH\cdot COOC_2H_5 + N_2.$$

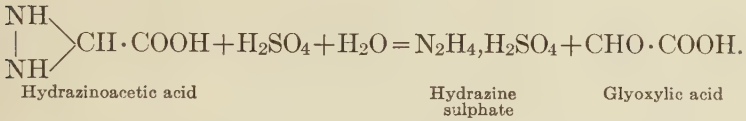
At a temperature close to its boiling-point ethyl diazoacetate loses all its nitrogen, with formation of ethyl fumarate:

$$2N_2CH\cdot COOC_2H_5 = 2N_2 + \begin{matrix}CH\cdot COOC_2H_5\\ \|\\ CH\cdot COOC_2H_5\end{matrix}.$$

II. In the second group of reactions the nitrogen is not evolved as gas, but one of the bonds between the diazo-group and carbon is severed, with formation of pyrazole-derivatives (**399**).

III. The third group comprises addition-reactions involving the

transformation of the double bond between the nitrogen atoms into a single bond. An example is the addition of hydrogen to form *hydrazinoacetic acid*, a compound decomposed by acids at the ordinary temperature into glyoxylic acid and a hydrazine salt:



The hydrogen atom of the CHN_2-group is replaceable by metals, sodium dissolving in ethyl diazoacetate with evolution of hydrogen.

PROTEINS.

246. *Proteins* are compounds of great importance in the animal and vegetable kingdoms, but of such complex structure as to render their chemical investigation a matter of extreme difficulty. Their great physiological importance is made apparent by the fact of the dry material in animal bodies, apart from the mineral constituents and fats, consisting almost wholly of proteins, by their being an essential constituent of each living plant-cell, and by their forming the most important part of human and animal food. An animal can exist without fats and carbohydrates for a protracted period, but its death is assured by the withdrawal of proteins from its nourishment.

The investigation of the proteins is rendered difficult not only by their complex structure, but also by the failure to obtain more than a few of them in crystalline form, and their invariable decomposition during distillation. As a result, advantage cannot be taken of these valuable aids in the isolation of individual substances. In addition, many proteins change very readily into other substances of the same group, and sometimes the distinctions between the different varieties are not well defined.

Sometimes proteins exhibit great differences in physical and chemical behaviour, a fact rendering it necessary first to state the general properties characteristic of them. They contain only five elements, and in composition do not differ much from one another, as the table indicates.

Carbon....	50–55 per cent.	Oxygen.....	19–24 per cent.
Hydrogen..	6·5–7·3 per cent.	Sulphur.....	0·3–5 per cent.
Nitrogen...	15–17·6 per cent.		

Those of one variety designated *phospho-proteins* also contain phosphorus.

The solutions of all proteins are optically active and lævorotatory. The proteins are colloids ("Inorganic Chemistry," 192), and therefore are unable to diffuse through parchment-paper. Often advantage is taken of this property in separating them from salts and other crystalloids (*loc cit.*). Some of them have been obtained crystalline, among them *serum-albumin*, but most of them are white amorphous powders without definite melting-points. Heat causes their carbonization, and the evolution of gases.

Many proteins can be "salted out" from solution, although there are exceptions. This "salting-out" is an important aid in identifying and separating the different varieties, and usually is effected by the aid of common salt or of magnesium sulphate. It is remarkable that all proteins can be salted out completely from their solutions in both

neutral and acidic liquids by saturation with ammonium sulphate. The albumins can be precipitated fractionally from aqueous solutions by gradually increasing the concentration of the ammonium-sulphate solution. The salt concentration required to initiate the precipitation of a protein is as characteristic for these organic compounds as is the solubility for a crystalline substance. A point important to remember is the dependence of this precipitation not only on the concentration of the salt but also on various other factors, such as the temperature and the concentration of the hydrogen ions, p_H. The salt concentration is only characteristic when these factors are known accurately. Salting-out at the ordinary temperature causes no change in the properties of the proteins, their solubilities after the operation being the same as before it.

247. Addition of dilute alcohol precipitates proteins unchanged from aqueous solution. Strong alcohol and boiling with water *coagulate* them. For each albumin there is a definite coagulation-point; in other words, each albumin coagulates at a definite temperature. The factors governing the salting-out process must also be taken into account in connexion with this reaction. For each type of protein there is a definite value of p_H best suited for coagulation, that for albumin being $p_H = 4 \cdot 8$. On coagulation, the differences in solubility between the proteins vanish, all being rendered insoluble in neutral solvents, and being brought into solution again only by dilute caustic alkalis or by mineral acids. A solution behaving exactly like the solutions thus obtained can be prepared by boiling uncoagulated albumins with a large excess of acetic acid or of caustic alkali.

In this process the albumins undergo a change known as *denaturation*. They cease to be coagulable by heat, but their composition remains unaltered. The products are designated *meta-proteins*. Formerly the product of a hydrolysis effected by alkali was termed an *albuminate* or *alkali-albumin*, and that formed by acid hydrolysis a *syntonin* or *acid-albumin*. The meta-proteins are insoluble in water, but soluble in dilute acids and alkalis. They are precipitated by neutralizing their solutions.

The proteins are precipitated from solution by various substances, either by coagulation or by the formation of compounds insoluble in water. Coagulation is effected by the addition of mineral acids, preferably nitric acid.

The formation of compounds insoluble in water is induced by the addition of salts of most of the heavy metals, especially cupric sulphate, ferric chloride, and an acidified solution of mercuric chloride. The proteins therefore behave like weak acids.

Some weak acids yield insoluble compounds with the proteins,

indicating these organic substances to have also a basic character. In this respect they exhibit complete analogy to their main decomposition-products, the amino-acids. Among such acids are *tannic acid*, *picric acid*, *phosphotungstic acid*, and others. The proteins are precipitated from solution completely by phosphotungstic acid, and this method, in addition to coagulation by boiling and precipitation by alcohol, is employed to separate dissolved proteins from solution.

Various *tests for proteins* are known, among them the following:

1. Millon's *reagent*, a solution of mercuric nitrate containing nitrous acid, yields at the boiling-point a red coagulated mass.

2. The *xanthoprotein-reaction* consists in the formation of a yellow coloration under the influence of warm nitric acid.

3. The *biuret-reaction* depends on the formation of a fine red to violet coloration on addition of potassium hydroxide to a protein, followed by that of a two per cent. solution of cupric sulphate drop by drop. This reaction derives its name from the fact of biuret under similar conditions giving the same coloration (**267**).

4. Addition of one drop of formaldehyde to a solution of five drops of egg-albumin in 3 c.c. of concentrated sulphuric acid produces a yellow coloration, changed to violet by addition of one drop of a solution of a nitrite. The reaction is due to the presence of *tryptophan*.

Nomenclature.

248. The Chemical Society of London, the English Physiological Society, the American Physiological Society, and the American Society of Biological Chemists have adopted the following system of nomenclature for the proteins.

1. **Protamines.**—They are the simplest members of the group. Examples are *salmine* and *sturine*, isolated from fish-sperm.

2. **Histones.**—They are more complex than the protamines, but probably each class gradually merges into the other. They are exemplified by the *histones* separated by Kossel from blood-corpuscles. Precipitability by ammonia is one of their distinguishing features.

3. **Albumins.**—*Egg-albumin*, *serum-albumin*, and *lact-albumin* are typical examples.

4. **Globulins.**—They differ from the albumins in solubility. They are salted out from solution more readily than the albumins. Examples are *serum-globulin*, *fibrinogen*, and such globulin-derivatives as *fibrin* and *myosin*.*

* The carbohydrate-radical separable in small quantities from many members of Classes 3 and 4 is probably not to be considered as a "prosthetic group": as it is

5. **Glutelins.**—Alkali-soluble proteins of vegetable origin. They are closely related to the globulins.

6. **Gliadins.**—Alcohol-soluble proteins found in the vegetable kingdom. The principal member of the group is *gliadin*, and ROSENHEIM has suggested designating the class by its name.

7. **Phospho-proteins.**—Examples are *vitellin*, *caseinogen* (the principal protein of milk), and *casein* (obtained from caseinogen by the action of rennet).*

8. **Sclero-proteins.**†—This class includes such substances as *gelatin*, *chondrin*, *elastin*, and *keratin*. The prefix indicates the skeletal origin of its members, and the insolubility of many of them.

9. **Conjugated Proteins.**‡—They are substances having the protein molecule united with a prosthetic group. The principal subdivisions are

a. NUCLEO-PROTEINS.—An example is *guanylic acid*, isolated from the pancreas, liver, spleen, and mammary gland.

b. CHROMO-PROTEINS.§—*Hæmoglobin* is a type.

c. GLUCO-PROTEINS.—They are exemplified by the *mucins*.

10. **Protein-derivatives.**¶—They comprise the products of protein-hydrolysis, and are classed in four divisions.

a. META-PROTEINS.—This group includes the substances formerly classed as "albuminates" or "alkali-albumins," and "syntonins" or "acid-albumins," obtained respectively by the action of an alkali or

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in the glucoproteins (9, *c*). The term *myosin* is restricted to the final product formed during *rigor mortis*. VON FÜRTH'S "soluble myogen-fibrin" should be called *soluble myosin*. The two chief proteins of the muscle-plasma are termed *paramyosinogen* and *myosinogen*.

* The prefix "nucleo-" frequently employed in relation to this class is incorrect and misleading. The American Societies include this group with the conjugated proteins (9). Since the phosphorus-containing radical is not eliminated from the phospho-proteins like a true prosthetic group, and their cleavage-products contain phosphorus, the English Societies prefer the arrangement indicated.

† This term replaces the word "albuminoid" in the limited sense adopted by most physiologists, but the American Societies retain the old name.

‡ The American Societies add "lecitho-proteins" to this class, but their English *confrères* object on account of the uncertainty as to whether these substances are mechanical mixtures, adsorption-compounds, or true chemical combinations.

§ The American Societies employ the term "Hæmoglobins" for chromoproteins.

¶ The American Societies include two additional classes in this group: "proteans," insoluble products apparently formed by the incipient action of water, very dilute acids, or enzymes; and "coagulated proteins," produced by the action of heat or of alcohol. They are of an ill-defined nature, and the English Societies consider it to be better not to single out for special mention a few of the infinite varieties of insoluble modifications exhibited by proteins.

an acid on albumins and globulins. The name meta-proteins is preferable because (1) they are derived from globulins as well as from albumins, and (2) the termination *ate* implies a salt.

b. Proteoses.—They include such substances as *albumose*, *globulose*, and *gelatose*.

c. Peptones.—Further products of hydrolysis resembling the proteins in answering the biuret-test, but differing from them in not being capable of precipitation from solution by salting.

d. Polypeptides.—Products of cleavage beyond the peptone stage containing two or more amino-acid-residues. Most of them are synthetic substances, but some of them have been separated from the products of protein-hydrolysis. Most of those hitherto prepared do not answer the biuret-test.

249. Particulars of some of the classes named are appended.

The *albumins* are the best known and most readily obtained of the proteins. All form well-defined crystals, and therefore they are probably among the few proteins known to be individual chemical compounds, although it has not been proved that these crystals are not mixed crystals containing two or more analogous individuals. They dissolve in water.

Their neutral solutions cannot be salted out with sodium chloride, magnesium sulphate, or a semi-saturated solution of ammonium sulphate. This property furnishes a method of separating them from the globulins always present with them.

The *globulins* are distinguished further from the albumins by their insolubility in water, although they dissolve in dilute neutral salt solutions, and in solutions of alkali-metal carbonates. At 30° they can be salted out completely by magnesium sulphate, and partly by sodium chloride. They have not been obtained crystalline.

The *phospho-proteins* contain phosphorus, and have a distinctly acidic character. All of them turn blue litmus red, and in the free state they are only slightly soluble in water, though their alkali-metal salts and ammonium salts are freely soluble. The solutions of their salts do not coagulate, and can be boiled without undergoing any change.

The *sclero-proteins* differ somewhat in character from the albumins. They exist in the animal economy only in the undissolved state, being the organic constituents of the skeleton and the epidermis. They include various substances such as *keratin*, *elastin*, *gelatin*, *collagen*, and *chondrin*.

Keratin is the principal constituent of the epidermis, hair, nails, hoofs, and feathers. It is particularly rich in sulphur, containing between four and five per cent. Its decomposition-products resemble

those of the albumins. With nitric acid it gives the xanthoprotein-reaction, the origin of the yellow colour developed by contact of nitric acid with the skin.

Elastin is the substance constituting the fibres of connective tissue. Its decomposition-products have the same qualitative composition as those obtained from the albumins. It is insoluble in dilute acids and caustic alkalis.

The *collagens* are the principal sclero-proteins of the animal body, and the main constituent of connective tissue such as bone-tissue and white fibrous tissue. In several respects they differ from the albumins; for they contain 17·9 per cent. of nitrogen; they have not an aromatic nucleus; and their hydrolysis does not yield tyrosine (**352**) as the chief decomposition-product, but glycine accompanied by leucine, aspartic acid, and glutamic acid.

Boiling with water transforms the collagens into *gelatin*. This substance is not precipitated from solution by nitric acid or by other mineral acids, but it is precipitated by mercuric chloride in presence of hydrochloric acid and by tannic acid.

Chondrin is obtained by extracting cartilage with boiling water, the solution gelatinizing as it cools. Acetic acid precipitates chondrin from solution. With boiling dilute acids chondrin yields a decomposition-product *chondrosin*, capable of reducing Fehling's solution. Chondrin is a derivative of gelatin and chondroitinsulphuric acid.

In the inferior orders of animal life a series of substances approximating more or less closely in chemical properties to the collagens and to elastin has been discovered. Among them is *spongin*, the principal constituent of sponges, a material much more stable than collagen towards a solution of sodium hydroxide or of barium hydroxide. Its complete hydrolysis by boiling with dilute sulphuric acid yields leucine and glycine, but no tyrosine, proving it to be a collagen.

Prolonged boiling with water converts silk into *fibroin*, a substance not decomposed by water even at 200°. *Sericin* or *silk-gum* also is formed.

Cornein is the organic constituent of coral. Its hydrolysis yields leucine, and an aromatic substance of unknown composition.

250. Nearly related to the albumins are the *conjugated proteins*, compounds of proteins with other substances, usually of a very complex nature. Like the albumins, they are insoluble in alcohol, and most of them are coagulated by it.

Nucleo-proteins derive their name from their rôle as the principal constituents of the cell-nuclei. They are combinations of proteins with phosphoric acid or *nucleic acids* (*Nucleus*, an important part of the cells

of animals or plants). A nucleic acid is phosphoric acid transformed by partial saturation through union with such basic substances as hypoxanthine, guanine, and xanthine. The composition of the nucleo-proteins differs considerably from that of the albumins; for they contain about 41 per cent. of carbon, 31 per cent. of oxygen, and 5·7 per cent. of phosphorus.

The nucleo-proteins have a markedly acidic character. They are soluble in water and are very soluble in caustic alkalis. They answer to the protein colour-tests.

Chromo-proteins are compounds of proteins with substances containing iron. *Hæmoglobin* is present in blood in very high proportion, dried human blood containing 90 per cent. of this dyestuff. It is a constituent of the red blood-corpuscles. It decomposes into *globin* and *hæmatin*. In the lungs it unites readily with the oxygen of respired air, yielding *oxyhæmoglobin*. This substance gives up its oxygen easily, thereby facilitating the oxidation-processes maintaining the heat of the animal body.

It unites with carbon monoxide to form *carbonyl-hæmoglobin*, a product unable to combine with oxygen. On this reaction the poisonous nature of carbon monoxide depends.

> Hæmoglobin also combines much more readily with carbon monoxide than with oxygen, the presence of only 0·1 per cent. of the monoxide in the air being attended by the conversion of 50 per cent. of the hæmoglobin into the carbonyl-derivative.

A mixture of acetic acid and sodium chloride converts oxyhæmoglobin into the hydrochloride of hæmatin, termed *hæmin*. It crystallizes in characteristic microscopic plates of a brown-red colour. The reaction furnishes a delicate test for blood.

Gluco-proteins are compounds of proteins and carbohydrates. They include the *mucins*, substances resembling the nucleo-proteins in their acidic character. They are insoluble in water, but soluble in a small proportion of lime-water or of an alkali solution. The liquid obtained is neutral, has a glutinous appearance, and is not coagulated by boiling. Unlike those of the albumins, these solutions are not precipitated by nitric acid. Boiling the mucins with acids or with caustic alkalis yields carbohydrates and either syntonins or peptones. The presence of the nitrogen-free carbohydrates makes the percentage-amount of nitrogen in the mucins considerably less than in the albumins, its value being between 11·7 and 12·3 per cent.

Meta-proteins are mentioned in **247**.

Proteoses and peptones can be obtained from all proteins by suitable

hydrolysis. They have the protein-character, being insoluble in alcohol, and answering the xanthoprotein-test and biuret-test (247, 2 and 3). They are produced during digestion by the action of gastric juice on proteins, and are to be regarded as intermediate products in the hydrolysis of proteins, the proteoses being nearer the proteins, and the peptones nearer the amino-acids.

The Structure of the Protein Molecule.

251. During last century experimental evidence of the complex structure of the protein molecule was accumulated, an important point being the great number of substances formed by the decomposition of albumin. Its dry distillation yields a black oil containing many nitrogen bases. Hydrogen cyanide, hydrogen sulphide, carbon dioxide, water, benzene and its homologues, and numerous other bodies also are formed. Both putrefaction and fusion with potassium hydroxide yield ammonia, hydrogen sulphide, volatile fatty acids such as butyric acid and valeric acid, amino-acids like leucine and tyrosine, scatole, ptomaines, *p*-cresol, and other products. Oxidation with various agents has rendered possible the isolation of hydrogen cyanide, carbonitriles, benzoic acid, numerous volatile fatty acids, and other substances.

New products have been gained by each fresh mode of attack, but the analytical methods employed have not shed any light on the structure of the protein molecule, for they yield chiefly amorphous and ill-defined substances. The first important step towards the solution of the problem was made by SCHÜTZENBERGER in obtaining only crystalline derivatives through heating proteins with an aqueous solution of barium hydroxide in an autoclave at 200° for several hours. After removal of the barium, the weight of the decomposition-products formed exceeded that of the initial proteins, proving the reagent to have effected addition of the elements of water, and thus to have hydrolyzed the proteins to crystalline derivatives.

It was impossible to effect complete separation of the very complex mixture obtained, but some of the less soluble constituents such as leucine and tyrosine were isolated. The presence in the reaction-product of a number of amino-acids was proved by its properties and the results of analysis. SCHÜTZENBERGER'S brilliant research was rendered more difficult by the necessity for making some hundreds of analyses. Its most important result was to identify the amino-acids as the foundation-stones of the proteins, just as the monoses constitute the bases of the polyoses (225). The fission-products obtained by earlier experimenters were formed by decomposition of the amino-acids,

252. Schützenberger did not succeed in separating the various amino-acids from the mixture obtained by his method of fractional crystallization; but the identification of the different amino-acids derivable from the individual proteins would be insufficient for a complete comprehension of the structure of the protein molecule, for the proportion of each acid also must be determined by separation of the complex mixture into its individual constituents. By esterification of the amino-acids (**241**) and fractional distillation *in vacuo* of the mixture of esters, Emil Fischer succeeded not only in isolating the principal constituents, but also in attaining an approximate insight into their relative proportions in the different proteins. His classical researches have enabled the products of protein-hydrolysis to be grouped in six divisions.

1. **Monobasic monoamino-acids.**—Glycine, alanine, 1-aminovaleric acid, leucine (**242**), and phenylalanine, $C_6H_5 \cdot CH_2 \cdot CHNH_2 \cdot COOH$.

2. **Dibasic monoamino-acids.**—Aspartic acid and glutamic acid or aminoglutaric acid.

3. **Diamino-acids.**—Ornithine and lysine (**243**). In the same category may be included arginine, obtained by addition of cyanamide to ornithine (**269**).

4. **Hydroxyamino-acids.**—Tyrosine (**352**) has been known for a long time. Of more recent date is *serine*, $CH_2OH \cdot CHNH_2 \cdot COOH$, synthesized from glycollaldehyde:

$$CH_2OH \cdot C\overset{H}{\underset{O}{}} + HCN \rightarrow CH_2OH \cdot CH\overset{CN}{\underset{OH}{}};$$
$$+NH_3 \rightarrow CH_2OH \cdot CHNH_2 \cdot COOH \text{ (240, 3)}.$$

This synthesis indicates the constitution of serine, and further confirmation is afforded by its reduction to alanine.

To this class also belongs the complicated *diaminotrihydroxydodecanic acid*, $C_{12}H_{26}O_5N_2$, a decomposition-product of casein.

5. **Compounds with a closed chain containing nitrogen.**—*α-Tetrahydropyrrolecarboxylic acid* or *proline*, and *hydroxytetrahydropyrrolecarboxylic acid* or *hydroxyproline*, are examples of such derivatives. *Tryptophan* (**403**), $C_{11}H_{12}O_2N_2$, contains a similar chain; and probably scatole (**403**), the cause of the characteristic odour of human fæces, is derived from this fission-product of proteins. Tryptophan is distinguished by the formation of a violet coloration or precipitate with bromine-water. The lævo-modification of *histidine*,

$$\begin{matrix} NH \cdot CH \\ | \quad\quad \diagdown \\ CH{=}N \quad\quad C \end{matrix} \cdot CH_2 \cdot CH(NH_2) \cdot COOH,$$

is a degradation-product of almost all albumins. Its racemic form has been synthesized, and has been resolved into its optical isomerides.

6. **Compounds containing sulphur.**—The only representative of this class is *cystine*, $C_6H_{12}O_4N_2S_2$, identified by Wollaston as early as the beginning of last century as the principal constituent of certain gall-stones. It has the formula

$$COOH \cdot CHNH_2 \cdot CH_2S—SCH_2 \cdot CHNH_2 \cdot COOH.$$

Reduction converts it into *cysteine*, $COOH \cdot CHNH_2 \cdot CH_2SH$, atmospheric oxidation of this derivative regenerating cystine.

The constitution of cystine has been ascertained through its formation from the benzoyl ester of serine with the benzoyl-group attached to nitrogen. Fusion with phosphorus pentasulphide converts the CH_2OH-group in this ester into a CH_2SH-group, and elimination of the benzoyl-group yields cysteine.

Emil Fischer found the hydrolysis of proteins to be effected more readily by boiling with concentrated hydrochloric acid or with sulphuric acid of 25 per cent. strength, than by Schützenberger's barium-hydroxide process.

Emil Fischer's ester-method has rendered possible the approximate quantitative estimation of the products of protein-hydrolysis. In reading the following brief summary of the results obtained it should be noted that usually not more, and often less, than 70 per cent. of the protein is recovered in the form of definite compounds, there being a considerable residue not identified on account of experimental difficulties.

Decomposition of some proteins yields a single amino-acid almost exclusively. Examples of such relatively simple proteins are *salmine* and *clupeine*, isolated by Kossel from the testicles of the salmon and herring respectively. Hydrolysis of the first yields 84·3 per cent. of arginine, and that of the second 82·2 per cent.

Usually, however, the proteins yield a series of amino-acids, the proportions of the individual constituents varying between wide limits. In most proteins leucine (242) is the principal constituent, as in hæmoglobin (250), keratin, and elastin (249). Only in fibroin and in gelatin (249) does glycine predominate. Of the dibasic amino-acids, aspartic acid (243) generally is present in small proportion. Casein (248, 7) contains a relatively large amount of *glutamic acid*. Tyrosine is the principal decomposition-product of fibroin, alanine and glycine being formed in smaller proportions. Cystine is an important constituent of keratin, as much as eight per cent. of it having been obtained from cow-hair. The hydrolysis of human hair also yields a large proportion of cystine.

The table summarizes the percentage-composition of a few proteins with respect to certain constituents.

	Hæmoglobin.	Casein.	Gelatin.	Keratin (from hair).	Fibroin.
Glycine	0	0	16·5	0·5	36·0
Alanine	4	1·5	0·8	1·6	21
Leucine	27·8	10·5	2·1	15·3	1·5
Aspartic acid	4·3	1·2	0·6	2·5	
Glutamic acid	1·7	15·5	14·0	27·3	
Arginine	5·2	4·8	9·3	2·7	4·0
Histidine	10·5	2·6	0.4		
Tyrosine	1·3	4·5		3·6	10·5
Proline	2·3	3·2	5·2		
Cystine	0·3	0·1		7·5	

253. Having elucidated the basis of the protein molecule, Emil Fischer applied himself to the solution of the greatest problem of organic chemistry, the synthesis of the proteins. For a long time the amino-acids of the protein molecule had been assumed to be united through their amino-groups, as in *glycylglycine*,

$$NH_2 \cdot CH_2 \cdot CO—NH \cdot CH_2 \cdot COOH.$$

In this substance the amino-group of one molecule of glycine has become attached to the carboxyl-group of another molecule, as in the formation of acid amides. This hypothesis was confirmed by the researches of Emil Fischer. By employing a number of synthetic methods, he succeeded in uniting various amino-acid-residues, and named the resulting compounds *polypeptides*. They display great analogy to the natural peptones (248, 10, *c*). Their synthesis proves them to have the structure indicated.

It is not possible to give here a detailed description of these synthetic methods, but a brief review will not be out of place. Heat converts the esters of amino-acids into anhydrides, with elimination of two molecules of alcohol, the reaction sometimes taking place even at the ordinary temperature:

$$\underset{\text{Glycine ethyl ester}}{2NH_2 \cdot CH_2 \cdot COOC_2H_5} = 2C_2H_5OH + NH\!<\!\begin{matrix}CO—CH_2\\CH_2—CO\end{matrix}\!>\!\underset{\substack{\text{Diketopiperazine}\\\text{(Glycine anhydride)}}}{NH}.$$

Under the influence of dilute potassium hydroxide, this anhydride takes up one molecule of water, yielding a *dipeptide*, glycylglycine:

$$NH\!<\!\begin{matrix}CO—CH_2\\CH_2—CO\end{matrix}\!>\!NH + H_2O = \underset{\text{Glycylglycine}}{NH_2 \cdot CH_2 \cdot CO—NH \cdot CH_2 \cdot COOH}.$$

With phosphorus pentachloride in acetyl-chloride solution, the carboxyl-group of a dipeptide is changed to COCl, and the residue of this acid chloride can be introduced into other amino-acids:

$$NH_2 \cdot CH_2 \cdot CO—NH \cdot CH_2 \cdot COCl + H_2N \cdot CH_2 \cdot COOC_2H_5 =$$
$$= NH_2 \cdot CH_2 \cdot CO—NH \cdot CH_2 \cdot CO—NH \cdot CH_2 \cdot COOC_2H_5 + HCl.$$

Saponification of this substance yields a *tripeptide*, and so on.

The polypeptides, especially from the *tetrapeptides* to the *octapeptides*, are very like the natural peptones, as is indicated by a short summary of the characteristics of both classes. Most of them are soluble in water, and insoluble in alcohol; but those less soluble dissolve readily in solutions of acids and of bases. Usually they melt above 200° with decomposition, have a bitter and insipid taste, and are precipitated by phosphotungstic acid. They answer the biuret-test (**247**, 3), the sensitiveness of the reaction for the polypeptides augmenting with increase in the length of the chain. Boiling with concentrated hydrochloric acid for about five hours effects complete hydrolysis. At the ordinary temperature they are stable towards alkalis. They are hydrolyzed by the action of pancreatic juice.

The highest polypeptide prepared by Emil Fischer is an *octadecapeptide* containing eighteen amino-acid residues, fifteen of them being glycine residues and three being leucine residues. It has all the characteristics enumerated, and had it been discovered first in nature, it would certainly have been classed as a protein.

This octadecapeptide has the molecular weight 1213, the value for most of the fats being much smaller, and for tristearin 891. It is the most complex substance of known structure hitherto obtained by synthesis. Abderhalden's researches have demonstrated the power of animal organisms to form proteins from a mixture of amino-acids in correct proportion, the basis of the proof being the continued existence of animals fed on such a mixture.

The mechanism of this synthesis of proteins must be wholly different from that involved in their production in the laboratory, and the same general rule is applicable to the synthetic formation of all natural products. Plants generate dextrose from carbon dioxide and water, and in presence of ammonia they form proteins and alkaloids. In the animal organism the synthesis of proteins is accompanied by that of fats. All these processes take place at the ordinary temperature, and without the aid of concentrated acids, phosphorus pentachloride, and other substances essential in artificial syntheses. Their mechanism is still very obscure. Probably the natural proteins are mixtures of various polypeptides hitherto inseparable.

The step-by-step decomposition of fibroin (249) also indicates the amino-acids in the proteins to have an amino-linking. With concentrated hydrochloric acid fibroin yields *sericoin*, a substance converted into a peptone by further boiling with the same acid. Pancreatic juice transforms this substance into tyrosine (352), and another peptone answering the biuret-test. After warming with barium-hydroxide solution this second peptone no longer answers this test, and a dipeptide, *glycylalanine*, can be isolated from the products of decomposition.

254. Apart from their magnitude, nothing is known about the molecular weights of the proteins. These substances being colloidal in solution, determinations of their molecular weights made by the aid of the lowering of the freezing-point or by that of osmotic pressure yield unreliable results. A method devised by SVEDBERG is based on measurements of the sedimentation-velocities of albumin solutions submitted to " ultra-centrifuging " at a speed of 10,000 or more revolutions per minute. For the albumin of hens' eggs it has indicated a molecular weight of 34,500, for hæmoglobin and serum-albumin twice as much, and for other proteins still higher values.

The subjoined reasoning enables a minimum value to be calculated for the molecular weight of hæmoglobin. This substance contains 0·366 per cent. of iron, and since its molecule cannot contain less than one atom of iron it is impossible for the molecular weight of hæmoglobin to be less than 16,700; but measurements of the osmotic pressure have indicated a molecular weight of 67,000, and this value accords with that given by SVEDBERG's method.

There is no gainsaying the unreliability of these figures. The close analogy between the higher polypeptides and many proteins indicates the probability of the chain of each protein molecule not containing many more than twenty amino-acid residues, these being capable of union to form larger complexes similar to those assumed for starch and cellulose.

Consideration of the differences in the nature and in the number alone of the amino-acids in the protein molecule indicates the theoretical possibility of an almost infinite variety of proteins. Assuming the protein molecule to contain twenty different amino-acid-residues, it can be represented by the scheme

$$A_{20}\cdot A_{19}\cdot A_{18}\ldots A_2\cdot A_1,$$

A being an amino-acid-residue. Each fresh grouping of these residues produces a new isomeride. According to the theory of permutations there are possible $20\times19\times18\times\ldots\times2\times1$ or approximately $2\cdot3\times10^{18}$ = 2·3 trillion groupings, and hence a like number of isomerides. For

other reasons this number must be increased greatly, the first of them being based on stereochemical considerations. Some amino-acids have asymmetric carbon atoms, and with a protein molecule containing n of them the number of stereisomerides possible is 2^n. Assuming the value of n in this example to be 10, each of the 2·3 trillion substances could exist in $2^{10} = 1024$ optically isomeric forms. The second reason is the existence of the group —CO·NH— also in the tautomeric form (235) —C(OH):N—. Obviously the number of possible isomerides is almost unlimited. It is so great as to make it feasible for each of the different kinds of living material to have its own individual protein, and for the infinite variety of forms found in organic nature to have originated partly as the result of isomerism in the protein molecule.

CYANOGEN DERIVATIVES.

Cyanogen, C_2N_2.

255. When mercuric cyanide, $Hg(CN)_2$, is heated, it decomposes into mercury and the gas *cyanogen*. The brown amorphous polymeric *paracyanogen*, $(CN)_x$, is formed simultaneously, but it is converted into cyanogen by heating at a high temperature. A better method for the preparation of cyanogen is the interaction of solutions of potassium cyanide and cupric sulphate. Cupric cyanide is formed, and at once decomposes into cuprous cyanide and cyanogen:

$$4KCN+2CuSO_4=2K_2SO_4+Cu_2(CN)_2+(CN)_2.$$

The reaction is analogous to that between potassium iodide and a solution of cupric sulphate to yield cuprous iodide and free iodine.

Cyanogen is related closely to oxalic acid, for heating ammonium oxalate with a dehydrator such as phosphoric oxide produces cyanogen. Inversely, dissolving cyanogen in hydrochloric acid adds four molecules of water and forms ammonium oxalate. These reactions prove cyanogen to be the nitrile of oxalic acid, its constitutional formula being

$$N{\equiv}C{-}C{\equiv}N.$$

In some respects cyanogen is analogous also to the halogens, as its preparation from potassium cyanide and cupric sulphate indicates. Moreover, potassium burns in cyanogen as in chlorine, with formation of potassium cyanide, KCN; and the passage of cyanogen into potassium hydroxide produces potassium cyanide, KCN, and potassium cyanate, KCNO, the process being analogous to the formation of potassium chloride, KCl, and potassium hypochlorite, KClO, by the action of chlorine on potassium hydroxide ("Inorganic Chemistry," **56**). Like silver chloride, silver cyanide is cheese-like in consistence, insoluble in water and dilute acids, and soluble in ammonium hydroxide.

Reduction with sulphurous acid converts cyanogen slowly into hydrogen cyanide, HCN, whereas the corresponding reduction of halogens to hydrogen halides takes place instantaneously.

At the ordinary temperature cyanogen is a gas of pungent odour, its boiling-point being $-20{\cdot}7°$. It is excessively poisonous. At high temperatures it is stable, but at the ordinary temperature its aqueous solution decomposes slowly, depositing a brown amorphous flocculent precipitate of *azulminic acid*. Cyanogen is inflammable, and burns with a peach-blossom coloured flame.

Hydrogen Cyanide, HCN.

256. *Hydrogen cyanide* ("prussic acid") is produced by passing a mixture of nitrogen and hydrogen over red-hot carbon heated electrically. An equilibrium is attained at one atmosphere of pressure and 2148°, corresponding with 4·7 per cent. of hydrogen cyanide.

The passage of sparks from an induction-coil through a mixture of acetylene and nitrogen produces hydrogen cyanide. Acetylene being obtainable by direct synthesis (**126**), this reaction furnishes another method of building up hydrogen cyanide from its elements. It is also formed from a mixture of methane with a large excess of nitrogen under the influence of an arc-discharge of high voltage, but the yield is small owing to the flame of the arc causing the decomposition of a large proportion of the hydrocarbon. Addition of a great excess of hydrogen, coupled with the instant absorption by alkali of the hydrogen cyanide produced, makes the yield almost quantitative.

Usually hydrogen cyanide is prepared by heating potassium ferrocyanide (**257**) with dilute sulphuric acid, the anhydrous substance being obtained by fractional distillation of the aqueous distillate. It is a colourless liquid with an odour resembling that of bitter almonds. It boils at 26°, and the solid melts at $-14°$.

Pure hydrogen cyanide is stable, but its aqueous solution decomposes with formation of brown amorphous insoluble substances. The residual solution contains various compounds, among them ammonium formate.

Like most cyanogen derivatives hydrogen cyanide is an excessively dangerous poison. The inhalation of hydrogen peroxide, or of air containing chlorine, is employed as an antidote. As with the mercury compounds ("Inorganic Chemistry," **283**), its toxic effect depends on the degree of ionization, a fact indicating the cyanogen ions to exert the poisonous action. Other evidence leads to the same conclusion, for the aqueous solution of potassium ferrocyanide contains no cyanogen ions, and the salt is not poisonous.

Hydrogen cyanide must be regarded as the carbonitrile of formic acid:

$$H{\cdot}COOH \rightarrow H{\cdot}CN.$$

Its formation by the distillation of ammonium formate, and the reverse transformation already cited of hydrogen cyanide into ammonium formate through addition of two molecules of water, favour this view. It finds support also in the formation of potassium cyanide from chloroform, $H \cdot CCl_3$, through warming with alcoholic ammonia and potassium hydroxide (**145**). Methylamine is obtained by reduction of hydrogen cyanide:

$$H \cdot C \equiv N + 4H = H_3C \cdot NH_2.$$

Hydrogen cyanide is one of the weakest acids, its aqueous solution having low electric conductivity.

Hydrogen cyanide can be obtained from *amygdaloside*, $C_{20}H_{27}O_{11}N$, a glucoside (**206**) present in bitter almonds and in other vegetable-products. In contact with water, amygdaloside is decomposed by the enzyme (**222**) *emulsin*, also a constituent of bitter almonds, into benzaldehyde, hydrogen cyanide, and dextrose:

$$\underset{\text{Amygdaloside}}{C_{20}H_{27}O_{11}N} + 2H_2O = \underset{\text{Benzaldehyde}}{C_7H_6O} + HCN + \underset{\text{Dextrose}}{2C_6H_{12}O_6}.$$

Substitution of maltase from yeast for emulsin yields only a single molecule of dextrose, *amygdalic nitrile glucoside*, $C_{14}H_{17}O_6N$, being formed simultaneously.

Cyanides.

257. The alkali-metal salts of hydrogen cyanide are manufactured chiefly for the lixiviation of gold and silver ores ("Inorganic Chemistry," **247** and **250**), three methods being employed in their preparation.

1. Wood-charcoal is heated with metallic sodium in a current of gaseous ammonia at temperatures between 500° and 600°, the primary product being *sodium cyanamide*, Na_2CN_2 (**260**). At a higher temperature this substance combines with carbon to form *sodium cyanide*, NaCN:

$$2NH_3 + 2Na + C = Na_2CN_2 + 3H_2;$$

$$Na_2CN_2 + C = 2NaCN.$$

2. Crude coal-gas also furnishes a source of hydrogen cyanide ("Inorganic Chemistry," **323**).

3. Spent wash (**43**) is evaporated, and the residue is submitted to dry distillation. Hydrogen cyanide is a constituent of the gaseous mixture evolved, and can be extracted by absorption with alkali.

Heating barium carbide in nitrogen yields barium cyanide:

$$BaC_2 + N_2 = Ba(CN)_2.$$

This reaction affords a means of preparing cyano-derivatives from atmospheric nitrogen.

Bucher's method consists in heating alkali-metal carbonates with carbon in a current of nitrogen, iron being employed as a catalyst. The first stage in the reaction is the reduction of the carbonate to metallic sodium, and the second the combination of the metal and carbon to form sodium carbide, Na_2C_2. The reaction temperature is about 1000°, and under these conditions the carbide absorbs nitrogen, giving an excellent yield of sodium cyanide, NaCN.

It is possible to prepare *ammonium cyanide*, $NH_4 \cdot CN$, in quantitative yield by passing a mixture of carbon monoxide and ammonia over thorium oxide heated to a temperature between 410° and 450°:

$$CO + 2NH_3 = NH_4 \cdot CN + H_2O.$$

The cyanides of the alkali-metals and of the alkaline-earth-metals, and mercuric cyanide, are soluble; other cyanides are insoluble. All have a great tendency to form complex salts, many of them, particularly those containing alkali-metals, being soluble in water and crystallizing well. The preparations and properties of some of these salts are described in "Inorganic Chemistry," 323.

Potassium cyanide, KCN, is obtained by heating potassium ferrocyanide, $K_4Fe(CN)_6$, to redness:

$$K_4Fe(CN)_6 = 4KCN + FeC_2 + N_2.$$

Potassium cyanide dissolves readily in water, and with difficulty in strong alcohol. It can be fused without undergoing decomposition. The aqueous solution is unstable, the potassium cyanide taking up two molecules of water. At the ordinary temperature the change is slow, but boiling accelerates it. Ammonia is eliminated, and potassium formate is produced:

$$KCN + 2H_2O = HCOOK + NH_3.$$

Potassium cyanide always has an odour of hydrogen cyanide, being decomposed by the carbon dioxide of the atmosphere into that compound and potassium carbonate.

The aqueous solution of potassium cyanide has a strongly alkaline reaction, the salt being hydrolyzed partially to hydrogen cyanide and potassium hydroxide ("Inorganic Chemistry," 66). Evidence of the existence of this decomposition is afforded also by the possibility of saponifying esters with a solution of potassium cyanide, this reaction furnishing a method of determining the degree of hydrolytic dissociation undergone by the salt.

Potassium ferrocyanide, $K_4Fe(CN)_6$, crystallizes in large sulphur-yellow crystals with three molecules of water. The application of gentle heat expels this water, leaving a white powder. The salt is not poisonous (**256**). On warming with dilute sulphuric acid it yields hydrogen cyanide. Heating with concentrated sulphuric acid evolves carbon monoxide, the sulphuric acid inducing the addition of two molecules of water to the hydrogen cyanide first formed, ammonia and formic acid being produced. The formic acid is decomposed immediately by the concentrated sulphuric acid into carbon monoxide and water (**81**). This method often is employed in the preparation of carbon monoxide.

Cyanic Acid, HCNO.

258. *Cyanic acid* is obtained by heating its polymeride *cyanuric acid* (**262**), and passing the vapour through a freezing-mixture. It is a colourless liquid, stable below 0°. If the flask containing it be removed from the freezing-mixture, so as to raise the temperature above 0°, vigorous ebullition ensues, sometimes accompanied by loud reports, and the liquid becomes converted into a white amorphous solid. This transformation was observed first by Liebig and Wöhler, and they named the product "insoluble cyanuric acid," or *cyamelide*. This substance is a polymeride of cyanic acid, and probably has the formula $(HCNO)_3$. Senier demonstrated the transformation-product to contain only about thirty per cent. of cyamelide, the remainder being cyanuric acid. The mixture can be separated by means of water, cyamelide being very sparingly soluble, and much less soluble than cyanuric acid.

The relationship subsisting between cyanic acid, cyanuric acid, and cyamelide is explained by the following considerations. At ordinary temperatures cyamelide is the stable modification. By cooling below 0°, the vapour of cyanuric acid yields cyanic acid, a transformation analogous to the condensation of phosphorus-vapour at low temperatures to the white variety, and not to the stable red modification. This phenomenon is due to the very small velocity of transformation of both the unstable forms at low temperatures. Above 0° the velocity of transformation of cyanic acid is much greater, and the polymeric stable cyamelide is formed, the process being accelerated considerably by its own calorific effect. Above 150° cyamelide is converted into the isomeric cyanuric acid. This transformation is analogous to that of rhombic sulphur into monoclinic sulphur, the transition-point being about 150°, although the process is so slow as to inhibit determination of the exact temperature. A similar slowness obscures the reverse process, the direct transformation of cyanuric acid into cyamelide, cyanuric acid at the ordinary temperature remaining

unchanged for an indefinite period, although it is an unstable modification. In this respect it is comparable with detonating gas ("Inorganic Chemistry," 13).

Above 0° an aqueous solution of cyanic acid changes rapidly into carbon dioxide and ammonia:

$$HCNO+H_2O=H_3N+CO_2.$$

The constitution of cyanic acid is unknown, but it yields two series of derivatives capable of being regarded as derived from *normal cyanic acid*, $C\begin{cases}OH\\N\end{cases}$, and from iso*cyanic acid*, $C\begin{cases}NH\\O\end{cases}$.

Cyanogen chloride, CNCl, can be considered to be the chloride of normal cyanic acid. It is a very poisonous liquid, freezing at $-1\cdot5°$, boiling at 13°, and with the density $1\cdot222$ at 0°. It can be obtained by the action of chlorine on hydrogen cyanide or potassium cyanide, and polymerizes readily to *cyanuric chloride*, $C_3N_3Cl_3$, especially in presence of hydrogen chloride. Cyanogen chloride is converted by potassium hydroxide into potassium chloride and potassium cyanate:

$$CNCl+2KOH=CNOK+KCl+H_2O.$$

259. *Esters of cyanic acid* have not been isolated. They are probably initial products of the action of sodium alkoxides on cyanogen chloride, since the polymeride *ethyl cyanurate*, $(CNOC_2H_5)_3$, can be separated readily from the reaction-product (**262**).

Esters of iso*cyanic acid* are well known, and are obtained by the action of alkyl halides on silver cyanate:

$$CO:N\boxed{Ag+I}C_2H_5=CO\cdot NC_2H_5+AgI.$$

The *iso*cyanic esters are volatile liquids with a powerful stifling odour. They also polymerize readily, yielding iso*cyanuric esters* such as $(CONC_2H_5)_3$ (**262**).

The constitution of the *iso*cyanic esters follows from their decomposition into carbon dioxide and an amine, effected by water, or better by dilute alkalis:

$$CO:N\cdot CH_3+H_2O=CO_2+NH_2\cdot CH_3.$$

This reaction was applied by Wurtz to the preparation of pure primary amines free from secondary and tertiary amines.

Primary amines can be obtained from acid amides by the action of bromine and potassium hydroxide (**96**). A more economical method is to

distil a mixture of the acid amide and bleaching-powder with a solution of calcium hydroxide. The mechanism of the reaction was investigated by HOOGEWERFF and VAN DORP. The first product was isolated, and found to be a substituted amide with bromine in union with nitrogen:

$$R \cdot CO \cdot NH_2 \rightarrow R \cdot CO \cdot NHBr.$$

Owing to the influence of the acid-residue, the hydrogen of the amino-group can be replaced by metals, and this replacement is facilitated considerably by the introduction of a bromine atom. The potassium hydroxide present causes the formation of a compound, $R \cdot CO \cdot NKBr$, it being unstable but capable of isolation. This potassium bromoamide readily undergoes an intramolecular transformation similar to the BECKMANN transformation (103):

$$\begin{matrix} R \cdot C \cdot OK \\ \| \\ Br \cdot N \end{matrix} \quad \text{changes to} \quad \begin{matrix} Br \cdot C \cdot OK \\ \| \\ R \cdot N \end{matrix} .$$

Potassium bromoamide

The transformation-product loses potassium bromide, with formation of an *iso*cyanic ester, $\begin{matrix} N \cdot R \\ \| \\ O \cdot C \end{matrix}$, decomposed by the water present into a primary amine and carbon dioxide.

Thiocyanic Acid, HCNS.

260. *Thiocyanic acid* (*sulphocyanic acid*) resembles cyanic acid in its properties, but is much more stable towards water. It can be obtained from barium thiocyanate by the action of the calculated proportion of dilute sulphuric acid. The anhydrous acid is formed at low temperature from concentrated sulphuric acid and a mixture of potassium thiocyanate and phosphoric oxide, the oxide being added to prevent the presence of excess of moisture. At 0° it forms a white crystalline solid, melting at about 5°, and quickly changing to a solid polymeride after removal from the freezing-mixture. When warmed with dilute sulphuric acid, thiocyanic acid takes up one molecule of water, and decomposes similarly to cyanic acid (258), with production of carbon oxysulphide, COS, instead of carbon dioxide:

$$HCNS + H_2O = H_3N + COS.$$

Potassium thiocyanate is obtained by boiling a solution of potassium cyanide with sulphur. Among other applications it is employed in VOLHARD'S method of silver-titration. When silver nitrate is added to a solution of potassium thiocyanate, *silver thiocyanate*, AgCNS, is deposited in

the form of a white cheese-like precipitate insoluble in dilute mineral acids. *Ferric thiocyanate*, $Fe(CNS)_3$, has a dark blood-red colour, and on its formation depends a test for ferric salts. The red colour is due to the non-ionized molecules $Fe(CNS)_3$, neither the ferric ion nor the thiocyanic ion being coloured in solution. The colour is intensified by diminution of the ionization by such a method as the addition of more of the ferric salt or of the thiocyanate. The red colour is removed by agitating the solution with ether, whereas ions cannot be extracted by this means. *Mercury thiocyanate* has the property of intumescing on decomposition by heat ("Pharaoh's serpents").

Like that of cyanic acid, the constitution of thiocyanic acid, is unknown. The two acids are alike in yielding two series of esters, those corresponding with thiocyanic acid being the *thiocyanic esters*, $C\leqslant^{S\cdot R}_{N}$, and those with *iso*thiocyanic acid the iso*thiocyanic esters*, $C\leqslant^{N\cdot R}_{S}$.

Thiocyanic esters are obtained by the action of alkyl iodides on the thiocyanates:

$$CN\cdot S\boxed{K+I}C_2H_5=CN\cdot SC_2H_5+KI.$$

They are liquids, insoluble in water, and characterized by a leek-like odour. The union of the alkyl-group in these compounds with sulphur is proved by the nature of the products obtained both by reduction and oxidation. Reduction yields mercaptans and hydrogen cyanide, methylamine being formed by the further reduction of that acid:

$$CN\cdot S\cdot C_2H_5+2H=CNH+H\cdot S\cdot C_2H_5.$$

Alkylsulphonic acids such as $C_2H_5\cdot SO_2OH$ (**60**) are produced by oxidation.

Under the influence of heat the thiocyanic esters are transformed into *iso*thiocyanic esters, distillation of allyl thiocyanate, $CN\cdot SC_3H_5$, effecting this change.

The *iso*thiocyanic esters are also termed *mustard-oils* after allyl *iso*thiocyanate, the substance imparting the odour and taste to mustard-seeds. The following reactions prove these compounds to contain an alkyl-group attached to nitrogen, and to have the constitution $C\leqslant^{N\cdot R}_{S}$. With concentrated sulphuric acid they add the elements of water, yielding a primary amine and carbon oxysulphide:

$$R\cdot N{:}CS+H_2O=R\cdot NH_2+COS.$$

They are converted by reduction into a primary amine and *trithiomethylene*, $(CH_2S)_3$, a substance probably generated through the polymerization of the thiomethylene, CH_2S, first formed, although the monothio-compound is unknown in the free state:

$$R\cdot N:CS+4H=R\cdot NH_2+CH_2S.$$

Cyanamide, $CN\cdot NH_2$, is obtained in various ways, including the action of ammonia on cyanogen chloride. It is a crystalline hygroscopic solid, and polymerizes readily. Its hydrogen atoms can be replaced by metals, silver yielding *silver cyanamide*, $CN\cdot NAg_2$. This substance is yellow and is insoluble in dilute ammonium hydroxide, wherein it differs from most silver compounds.

When calcium carbide is heated to redness in a current of nitrogen, *calcium cyanamide* is formed:

$$CaC_2+N_2=CN\cdot NCa+C.$$

The absorption of nitrogen is facilitated greatly by addition of ten per cent. of calcium chloride. This compound can be obtained also by heating lime and carbon to a red heat in an atmosphere of nitrogen. The crude product is termed "Lime-nitrogen" and finds application as an artificial fertilizer, being decomposed slowly into ammonia and calcium carbonate by water at the ordinary temperature:

$$CaCN_2+3H_2O=2NH_3+CaCO_3.$$

The reaction is accelerated considerably by heating under pressure. By this method ammonia can be produced directly from the nitrogen of the atmosphere.

Fulminic Acid.

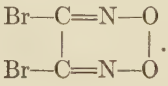
261. Salts of *fulminic acid* are obtained by the interaction of mercury or silver, nitric acid, and alcohol in certain proportions. The most important is *mercuric fulminate*, $HgC_2O_2N_2$, a product prepared on a large scale, and employed for filling percussion-caps and for other purposes. Gun-cotton can be exploded by the detonation of a small proportion of this substance (**228**); and as it exerts a similar effect on other explosives, the so-called "fulminating mercury" plays an important part in the application of such substances.

Silver fulminate, Ag(CNO), is much more explosive than the mercury salt, and hence is not employed technically. The explosion of these salts has a *brisant* (**154**), though only local, effect; and this characteristic enabled

Howard, the discoverer of mercuric fulminate, to explode a small quantity in a balloon without injury to the machine, the only effect being to shatter the leaden shells containing the explosive.

Free fulminic acid is a very unstable and volatile substance. It has an odour resembling that of hydrogen cyanide, and is excessively poisonous.

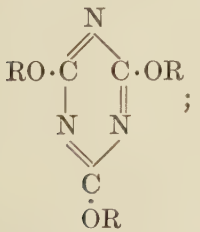
According to Nef, the formula of fulminic acid is C=N·OH, containing a bivalent carbon atom. With acetyl chloride mercuric fulminate yields a compound of the formula $CH_3 \cdot CO(CNO)$. In presence of hydrochloric acid the fulminate takes up the elements of water, with formation of hydroxylamine and formic acid. It is converted by bromine into a compound, $Br_2C_2O_2N_2$, with the constitutional formula



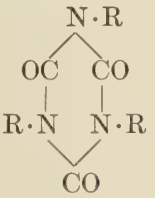
Cyanuric Acid and *iso*Cyanuric Acid.

262. *Cyanuric bromide*, $C_3N_3Br_3$, is obtained by the interaction of potassium ferricyanide and bromine at 220°. By heating with water, the bromide is converted into *cyanuric acid*, $(CNOH)_3$, a substance usually prepared by the action of heat on urea (**267**). Two series of esters are derived from this acid, the *normal cyanuric esters* and the iso*cyanuric esters*, the first being termed "*O*-esters," and the second "*N*-esters."

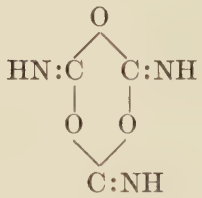
The normal cyanuric esters are obtained by the action of sodium alkoxides on cyanuric chloride or bromide. The formation of alcohol and cyanuric acid by saponification proves the alkyl-group in these esters to be in union with oxygen. For this reason constitutional formula I is assigned to them:



I.



II.



III.

The *iso*cyanuric esters are produced by heating silver cyanurate with alkyl iodides. Their alkyl-groups are attached to nitrogen, for boiling such an ester with alkali gives a primary amine and carbon dioxide, a decomposition in accord with constitutional formula II.

The *O*-esters are formed from alkyl iodides and silver cyanurate at the ordinary temperature, but their conversion into the *N*-esters by heat explains the difference between the product obtained at the ordinary temperature and that produced at elevated temperatures.

Important evidence in favour of the imino-formula for cyanuric acid was furnished by Chattaway and Wadmore's replacement of the metal in potassium cyanurate by chlorine. They regard the compound formed as $(O:C:N\cdot Cl)_3$.

Formula III, containing imino-groups, possibly represents the structure of cyamelide.

DERIVATIVES OF CARBONIC ACID.

263. *Carbonic acid*, H_2CO_3 or $CO(OH)_2$, is not known in the free state, but is supposed to exist in the solution of carbon dioxide in water. It decomposes very readily into its anhydride carbon dioxide, and water. It is dibasic, and generally is described with its salts in text-books of inorganic chemistry ("Inorganic Chemistry," **181**). Some of its organic derivatives are considered in this chapter.

Carbonyl Chloride, $COCl_2$.

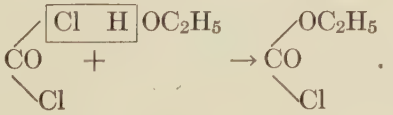
Carbonyl chloride (*phosgene*) is prepared by heating chlorine and carbon monoxide. An equilibrium,

$$Cl_2 + CO \rightleftarrows COCl_2,$$

is attained, corresponding at 505° with about 67 per cent. of dissociation. It was named phosgene (φῶς, light; γεννάω, to produce) by J. Davy in 1811, its formation by this means being thought to be contingent on the presence of sunlight, a view since proved to be incorrect. Carbonyl chloride is a gas with a powerful stifling odour. The gas liquefies at 8·2°, the liquid formed freezing at −126°, and having the density 1·434 at 0°. It dissolves readily in benzene, and the solution is employed in laboratory and industrial syntheses.

> At the ordinary temperature carbonyl chloride is decomposed by ultraviolet light, especially by the rays of short wave-length, into carbon monoxide and chlorine, the mechanism of the process being similar to that described in "Inorganic Chemistry," **78**. Carbon monoxide and chlorine also combine under the influence of this light, indicating the attainment of an equilibrium.

The reactions of carbonyl chloride demonstrate it to be the chloride of carbonic acid. It is decomposed slowly by water, yielding hydrogen chloride and carbon dioxide. With ethyl alcohol at the ordinary temperature its first product is *ethyl chlorocarbonate*:



More prolonged contact with that alcohol, and also the action of sodium ethoxide, produce *diethyl carbonate*, $CO(OC_2H_5)_2$. Ammonia replaces the two chlorine atoms in carbonyl chloride by amino-groups, with formation of the amide of carbonic acid, *urea*, $CO(NH_2)_2$ (**266**). All these reactions are characteristic of acid chlorides.

The chlorocarbonic esters, also termed *chloroformic esters*, are colourless liquids of strong odour, and distil without decomposition. They are employed for the introduction into compounds of the group $—COOC_2H_5$ (**235**).

The carbonic esters also are liquids, but are characterized by the possession of an ethereal odour. They are insoluble in water, and are saponified very readily.

Carbon Disulphide, CS_2.

264. *Carbon disulphide* is manufactured synthetically by passing sulphur-vapour over red-hot carbon. The crude product has a very disagreeable odour removable by distillation from fat. The pure product is an almost colourless, highly refractive liquid of ethereal odour. It is insoluble in water, boils at 46°, and at 20° has the density 1·262. Carbon disulphide is poisonous, and being highly inflammable it must be handled with great care. It is an excellent solvent for fats and oils, and finds extensive application in the extraction of these substances from seeds. It is employed also in the vulcanization of india-rubber.

Although endothermic, carbon disulphide is a stable compound, and resists the action of heat ("Inorganic Chemistry," **115**). Its vapour can be exploded by means of mercuric fulminate. The halogens have little action on it at the ordinary temperature; but in presence of a halogen-carrier chlorine or bromine can effect substitution, with production of carbon tetrachloride or tetrabromide.

As an anhydrosulphide carbon disulphide resembles carbon dioxide in being the anhydride of an acid. With alkali-metal or alkaline-earth-metal sulphides it yields *trithiocarbonates*:

$$BaS + CS_2 = BaCS_3.$$

Barium trithiocarbonate

The barium salt is yellow, and dissolves in cold water with difficulty. The addition of dilute acids to its salts gives free *trithiocarbonic acid*, H_2CS_3, as an unstable oil. The potassium salt is employed in the destruction of vine-lice.

The potassium salt of *xanthic acid* is formed by the action of potassium ethoxide on carbon disulphide:

$$CS_2+KOC_2H_5=CS\begin{matrix}OC_2H_5\\SK\end{matrix}.$$

This change is effected by agitating carbon disulphide with a solution of potassium hydroxide in absolute ethyl alcohol, *potassium xanthate* separating in the form of yellow glittering needles. Free xanthic acid is very unstable, for within a few minutes of its liberation from its potassium salt in the form of an oil it begins to develop heat, and then with vigorous ebullition decomposes into ethyl alcohol and carbon disulphide. This reaction exemplifies the phenomenon of *autocatalysis*, for it is accelerated by the alcohol as it is liberated.

Xanthic acid owes its name (ξανθός, yellow) to its yellow cuprous salt, produced by the spontaneous transformation of the brownish-black cupric salt precipitated from a solution of cupric sulphate by the addition of a xanthate.

Carbon Oxysulphide, COS.

265. *Carbon oxysulphide* is a colourless, odourless, inflammable gas: and is obtained by the action of hydrogen sulphide on *iso*cyanic esters,

$$2CO\cdot NC_2H_5+H_2S=COS+CO(NHC_2H_5)_2.$$

Its formation from *iso*thiocyanic esters is mentioned in **260.** It is produced also by passage of a mixture of carbon monoxide and sulphur-vapour through a tube at a moderate heat.

Carbon oxysulphide is absorbed somewhat slowly by alkalis. It yields salts with metallic alkoxides, and these compounds can be regarded as derived from carbonates by simultaneous exchange of oxygen for sulphur:

$$COS+C_2H_5\cdot OK=CO\begin{matrix}OC_2H_5\\SK\end{matrix}.$$

Urea, $CO<\begin{matrix}NH_2\\NH_2\end{matrix}$.

266. *Urea* owes its name to its occurrence in urine, as the final decomposition-product of the proteins in the body.

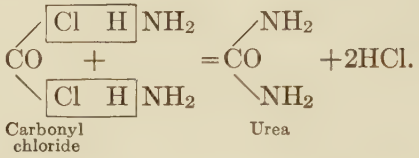
In twenty-four hours an adult excretes about 1,500 grammes of urine, containing approximately two per cent. of urea, the daily production of this substance amounting to about thirty grammes. To obtain urea from urine, the liquid must undergo a preliminary concentration by evaporation. On addition of nitric acid, *urea nitrate*, $CO(NH_2)_2,HNO_3$, (**267**) is precipitated. Owing to impurities it has a yellow colour, removable by dissolving the precipitate in water and oxidizing with potassium permanganate.

Urea is liberated from the solution of the nitrate by the action of barium carbonate:

$$2(\underset{\text{Urea nitrate}}{CON_2H_4,HNO_3})+BaCO_3=2CON_2H_4+Ba(NO_3)_2+H_2O+CO_2.$$

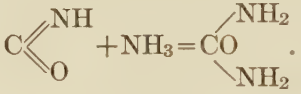
Solution in concentrated alcohol serves to isolate the organic compound from the mixture of urea and barium nitrate left by evaporation to dryness.

On account of its formation along with cyanuric acid and cyamelide from the chloride of carbonic acid, carbonyl chloride, $COCl_2$, urea is to be regarded as the amide of that acid. This reaction proves its constitution (263):



A confirmation of this view of the structure of urea is its formation by the action of ammonia on diethyl carbonate.

Urea is produced by addition of ammonia to *iso*cyanic acid:



Ammonium *iso*cyanate dissolved in water is transformed into urea during evaporation of the solution. By this method Wöhler effected his classic synthesis of urea by heating a mixture of potassium cyanate and ammonium sulphate in solution (1).

This reaction has an important bearing on the history of organic chemistry and has been studied in detail by James Walker and Hambly. Their researches revealed the occurrence also of the reverse transformation of urea into ammonium *iso*cyanate, for addition of silver nitrate to a solution of pure urea in boiling water yields a precipitate of silver cyanate. An equilibrium is attained:

$$\underset{\text{Urea}}{CO(NH_2)_2} \rightleftarrows \underset{\substack{\text{Ammonium}\\ \textit{iso}\text{cyanate}}}{CON{\cdot}NH_4}.$$

When this equilibrium is reached, the solution contains a small percentage only of *iso*cyanate. It is almost independent of the temperature, proving the transformation of the systems into one another to be accompanied by only slight calorific effect (94).

Urea is manufactured as an artificial fertilizer by heating ammonium carbonate under pressure at temperatures between 130° and 140°, each molecule of the salt losing two molecules of water:

$$CO(ONH_4)_2 = CO(NH_2)_2 + 2H_2O.$$

*iso*Cyanic esters are decomposed by water, with formation of primary amines and carbon dioxide (**259**). Contact of the primary amine formed with a second molecule of *iso*cyanic ester induces an addition-reaction, with production of a *symmetrical dialkylurea*:

$$CO{:}NR + H_2NR' = CO\begin{matrix}\diagup NHR \\ \diagdown NHR'\end{matrix}.$$

This process is a general method for preparing symmetrical dialkylureas.

A *monoalkylurea* is obtained by the action of ammonia, instead of an amine, on an *iso*cyanic ester.

Unsymmetrical dialkylureas, $CO\begin{matrix}\diagup NRR' \\ \diagdown NH_2\end{matrix}$, are prepared by the action of *iso*cyanic acid on secondary amines. The method of procedure is analogous to that employed in Wöhler's synthesis of urea, and consists in warming a solution of the *iso*cyanate of a secondary amine:

$$CONH\cdot NHRR' = CO\begin{matrix}\diagup NRR' \\ \diagdown NH_2\end{matrix}.$$

The unsymmetrical dialkylureas are converted by 100 per cent. nitric acid into nitro-compounds discovered by Franchimont, and termed *nitroamines* (**270**):

$$\left.\begin{matrix}(CH_3)_2N\cdot \\ +NO_2\cdot\end{matrix}\right|\begin{matrix}CONH_2 \\ OH\end{matrix} \rightarrow (CH_3)_2N\cdot NO_2\cdot$$

267. Urea crystallizes in elongated prisms, the crystals resembling those of potassium nitrate. They are very soluble in water, and melt at 132°. Like the amines, urea forms salts by addition of acids, but only to one amino-group. The *nitrate*, CON_2H_4,HNO_3, and the *oxalate*, $2CON_2H_4,C_2H_2O_4$, dissolve with difficulty in solutions of the corresponding acids.

In some of its reactions, notably in certain condensation-processes, the behaviour of urea corresponds with the structure $C(=NH)(OH)(NH_2)$. An ether of this iso*urea* is obtained by addition of methyl alcohol to cyanamide, the reaction being facilitated by the presence of hydrogen chloride:

$$N{\equiv}C{-}NH_2 + HOCH_3 = C(OCH_3)(=NH){-}NH_2 .$$

Cyanamide — Methyl*iso*urea

This method of formation indicates the constitution of the compound. A confirmatory reaction is the production of methyl chloride by heating methyl*iso*urea with hydrogen chloride. This transformation indicates the methyl-group not to be in union with nitrogen, for under similar conditions *methylurea*, $CO(NH_2)(NHCH_3)$, loses methylamine, $CH_3 \cdot NH_2$.

When heated, urea melts; it then begins to evolve a gas, consisting principally of ammonia, but also containing carbon dioxide; after a time the residue solidifies. The initial reaction is the loss by two molecules of urea of one molecule of ammonia, with production of *biuret*:

$$CO(NH_2)(NH_2H) \quad H_2N(HN)CO = NH_2 \cdot CO \cdot NH \cdot CO \cdot NH_2 + NH_3.$$

Biuret

Biuret is a crystalline substance melting at 190°. When cupric sulphate and potassium hydroxide are added to its aqueous solution, it gives a characteristic red to violet coloration ("biuret-reaction").

On further heating, biuret unites with a molecule of unaltered urea, eliminating ammonia and forming cyanuric acid (**262**):

$$H|NH \cdot CO \cdot NH \cdot CO \cdot NH|H = \begin{matrix} & NH & \\ OC & & CO \\ | & & | \\ HN & & NH \\ & CO & \end{matrix} + 2NH_3.$$
$$H_2N \cdot CO \cdot NH_2$$

Like the acid amides, urea is decomposed by heating with bases, yielding carbon dioxide and ammonia.

Derivatives of Carbamic Acid.

268. *Carbamic acid,* $NH_2 \cdot CO \cdot OH$, is the semi-amide of carbonic acid. It is unknown in the free state, existing only as salts, esters, and chloride. *Ammonium carbamate* is formed by the union of dry carbon dioxide with dry ammonia:

$$CO_2 + NH_3 = C(=O)(OH)(NH_2) \; ; \quad + NH_3 = C(=O)(OHNH_3)(NH_2) \; .$$

Ammonium carbamate

With an ammoniacal solution of calcium chloride carbon dioxide does not yield a precipitate, the *calcium carbamate,* $CO(Oca^*)(NH_2)$, produced being soluble in water.

When the salts of carbamic acid are heated in solution, they take up the elements of water readily to form carbonates.

The esters of carbamic acid are termed *urethanes.* They are formed by the action of ammonia or amines on the esters of carbonic acid or of chlorocarbonic acid:

$$CO(\boxed{OC_2H_5 + H}NH_2)(OC_2H_5) = CO(NH_2)(OC_2H_5) + C_2H_5OH;$$

Diethyl carbonate — Urethane

$$CO(\boxed{Cl + H}NH_2)(OC_2H_5) \rightarrow CO(NH_2)(OC_2H_5) \; .$$

Ethyl chloro-carbonate

Urethanes are produced also by the action of alcohol on *iso*cyanic esters:

$$C(=O)(NCH_3) + HOC_2H_5 = C(=O)(OC_2H_5)(NHCH_3) \; .$$

Another mode of preparing urethanes involves the boiling of acid azides (**97**) with alcohol:

$$R \cdot CON_3 + C_2H_5OH = R \cdot NHCOOC_2H_5 + N_2.$$

---

* $ca = \frac{1}{2}Ca$.

Since the azides are obtained easily from the corresponding acids, and the urethanes yield the corresponding amines readily, the carboxyl-group can be replaced by the amino-group:

$$\underset{\text{Acid}}{R\cdot COOH} \rightarrow \underset{\text{Ester}}{R\cdot COOC_2H_5} \rightarrow \underset{\text{Hydrazide}}{R\cdot CONHNH_2} \rightarrow \underset{\text{Azide}}{R\cdot CON_3} \rightarrow$$

$$\rightarrow \underset{\text{Urethane}}{R\cdot NHCOOC_2H_5} \rightarrow \underset{\text{Primary amine}}{R\cdot NH_2}.$$

Urethanes distil without decomposition. Ordinary urethane, $CO\begin{matrix}OC_2H_5\\NH_2\end{matrix}$, melts at 51°, and dissolves in water very readily. Boiling with bases decomposes it into ethyl alcohol, carbon dioxide, and ammonia. Concentrated nitric acid transforms it into *nitrourethane*, $C_2H_5O\cdot CO\cdot NH\cdot NO_2$, a substance converted by careful hydrolysis into *nitroamine*, $NH_2\cdot NO_2$.

Guanidine, CH_5N_3.

269. *Guanidine* is formed by the interaction of ammonia and orthocarbonic esters, or chloropicrin, CCl_3NO_2, obtained by nitrating chloroform. Probably the change involves the initial addition of four amino-groups to the carbon atom, the compound formed losing one molecule of ammonia:

$$\underset{\substack{\text{Tetraethyl ortho-}\\\text{carbonate}}}{C(OC_2H_5)_4} \rightarrow C(NH_2)_4;\ -NH_3 \rightarrow \underset{\text{Guanidine}}{C(=NH)(NH_2)_2}.$$

This method of preparing guanidine establishes the constitutional formula indicated. Further evidence is afforded by its synthesis by heating cyanamide with an alcoholic solution of ammonium chloride:

$$C\equiv N\cdot NH_2 + NH_4Cl = \left(C(=NH)(NH_2)_2\right)HCl.$$

Guanidine is a colourless crystalline substance, and absorbs moisture and carbon dioxide from the atmosphere readily. Unlike urea with a neutral reaction, it is a strong base. The strengthening of the basic character, occasioned by exchange of carbonyl-oxygen for an imino-group, is worthy of notice. Guanidine yields many well-defined crystalline salts.

Arginine, $C_6H_{14}O_2N_4$, is obtained from proteins, and is an important derivative of guanidine. It can be synthesized by the action of cyanamide on ornithine (**243**):

$$\underset{\text{Ornithine}}{COOH\cdot CH(NH_2)\cdot (CH_2)_3\cdot NH_2} + \underset{\text{Cyanamide}}{CN_2H_2} =$$

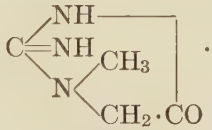
$$= \underset{\text{Arginine}}{COOH\cdot CHNH_2\cdot (CH_2)_3NH\cdot C(:NH)\cdot NH_2}$$

The cyanamide is added at the 4-NH_2-group, as represented in the equation, so that arginine is 1-*amino*-4-*guanino*-n-*valeric acid*.

The muscular tissue of the human body contains about 0.3 per cent. of *creatine*. Its structure is indicated by its synthetic formation from *methylglycine* or *sarcosine* and cyanamide:

$$C(NH_2)\equiv N + HN(CH_3)(CH_2\cdot COOH) = \underset{\text{Creatine}}{C(NH_2)=NH\cdot N(CH_3)(CH_2\cdot COOH)}$$

By elimination of one molecule of water, creatine is converted into *creatinine*,



Creatinine

Nitroamines.

270. The *nitroamines* are compounds with a nitro-group having its nitrogen atom in union with another nitrogen atom, and they have the general formula

$$\begin{matrix} R \\ R' \end{matrix} > N\cdot NO_2.$$

They have been studied chiefly by Franchimont and his students, and these experimenters have devised various methods for their preparation.

The preliminary step in the transformation of a primary amine into a nitroamine, $R\cdot NH\cdot NO_2$, is to convert it into an acid amide, $R'\cdot CO\cdot NH\cdot R$.

Cooled, absolute nitric acid changes this amide into a compound of the formula

$$R'\cdot CO\cdot N<\begin{matrix}NO_2\\R\end{matrix}.$$

The acid residue can be eliminated from this substance by the action of ammonia.

The monoalkylurethanes, $R\cdot NH\cdot CO\cdot OC_2H_5$, are specially suited for nitration and the subsequent preparation of the primary nitroamines by the action of ammonia on the products. Guanidine also can be transformed readily into *nitroguanidine*,

$$HN:C<\begin{matrix}NH\cdot NO_2\\NH_2\end{matrix},$$

a substance soluble with difficulty in cold water, and therefore precipitated on pouring its solution in the acid into water.

The secondary nitroamines, $R_2N\cdot NO_2$, can be prepared from the secondary amines by a preliminary transformation by means of cyanic acid into unsymmetrical dialkylureas, $R_2NCO\cdot NH_2$, followed by the action of absolute nitric acid on these products, the $CONH_2$-group being replaced by a nitro-group.

At the ordinary temperature the nitroamines are partly liquid and partly crystalline, but most of them exhibit a marked capacity for crystallization. Their density is somewhat greater than 1. The primary nitroamines have an acidic reaction, and form salts. Heating induces many nitroamines to undergo an explosive decomposition.

The quantitative elimination as nitrous oxide of all the nitrogen of the primary nitroamines is effected by warming them with dilute sulphuric acid, an alcohol being formed simultaneously. It is possible to explain this change by assuming the nitroamines to undergo a preliminary transformation into a tautomeric form:

$$R\cdot NH\cdot NO_2 \rightarrow R\cdot N:NO\cdot OH \rightarrow R\cdot OH+N_2O.$$

On careful reduction the nitroamines yield hydrazines, a reaction indicating their constitution.

URIC-ACID GROUP.

271. *Uric acid,* $C_5H_4O_3N_4$, derives its name from its presence in small proportion in urine, and is the nucleus of an important group of urea derivatives. It is related closely to the *ureïdo-acids* and the *acid-ureïdes* (*ureïdes*), these substances being amino-acids and acid amides with the urea-residue, $NH_2 \cdot CO \cdot NH—$, instead of the NH_2-group.

Alloxan, $C_4H_2O_4N_2,H_2O$, is an important decomposition-product of uric acid, being obtained by its oxidation with nitric acid, and also by other methods. It is *mesoxalylurea*, for alkalis add two molecules of water and produce urea and mesoxalic acid:

$$\begin{array}{lll} CO——NH+OHH & CO\cdot OH & NH_2 \\ | \quad\quad | & | & | \\ CO \quad\quad CO & =CO & +CO. \\ | \quad\quad | & | & | \\ CO——NH+OHH & CO\cdot OH & NH_2 \end{array}$$

Alloxan — Mesoxalic acid

The elimination of the molecule of water of crystallization from alloxan is as difficult as from mesoxalic acid (**234**). Like this acid, the anhydrous substance is coloured yellow, but the crystalline hydrate is colourless.

Carbon dioxide and parabanic acid are formed by the oxidation of alloxan with nitric acid. Parabanic acid has the structure $\begin{array}{l} CO—NH \\ | \quad\quad \rangle CO, \\ CO—NH \end{array}$ and may therefore be regarded as oxalylurea.

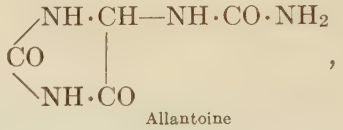
Alloxan is converted by reduction into *alloxantine*:

$$2C_4H_2O_4N_2+2H=C_8H_6O_8N_4.$$

Alloxantine

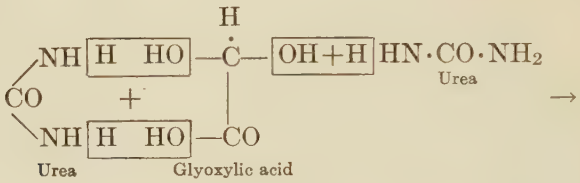
Alloxantine is formed also from uric acid directly by evaporating it to dryness with dilute nitric acid. With ammonia it forms a purple-red dye, *murexide,* $C_8H_8O_6N_5$. The formation of murexide is employed as a test for uric acid. Alloxantine dissolves with difficulty in cold water, and gives a blue colour with barium hydroxide solution. The constitution of these compounds has not been elucidated.

Allantoine, $C_4H_6O_3N_2$, is formed in the oxidation of uric acid with potassium permanganate, a fact with an important bearing on the constitution of this acid. Allantoine has the structure

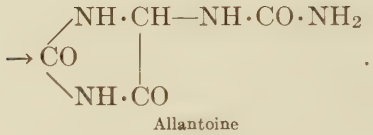


Allantoine

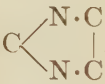
for it can be obtained synthetically by heating glyoxylic acid with urea:

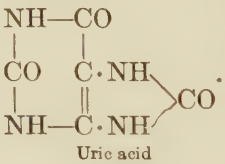


Urea Glyoxylic acid



Allantoine

The formation of alloxan and allantoine from uric acid gives an insight into the constitution of that acid, the production of the first indicating the presence of the complex , and that of the second the presence of two urea-residues, with the complex  . These groupings find expression in the structural formula

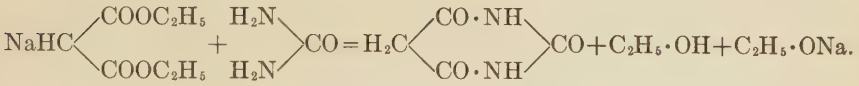


Uric acid

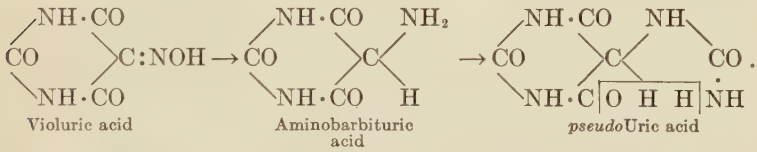
This formula accords also with the other chemical properties of uric acid.

The following synthesis affords confirmation of the accuracy of the constitution indicated. When heated in alcoholic solution, ethyl

sodiomalonate and urea combine to form *malonylurea* or *barbituric acid*:



Under the influence of nitrous acid, this substance yields *violuric acid*, an *iso*nitroso-compound also obtainable from alloxan and hydroxylamine. Reduction converts violuric acid into *aminobarbituric acid* or *uramil*, a substance resembling the amines in adding one molecule of *iso*cyanic acid on contact with potassium cyanate, forming pseudo*uric acid*:



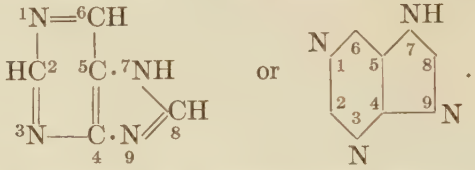
*pseudo*Uric acid differs from uric acid only in containing the elements of another molecule of water. Boiling with a large excess of twenty per cent. hydrochloric acid eliminates this molecule of water as indicated in the formula, the process yielding a substance with the constitution assigned to uric acid, and identical with that compound.

Uric acid dissolves with difficulty in water; but it is soluble in concentrated sulphuric acid, and is precipitated from the solution by addition of water. It forms two series of salts, by exchange of either one or two hydrogen atoms for metals. *Normal sodium urate*, $C_5H_2O_3N_4Na_2,H_2O$, is much more soluble in water than *sodium hydrogen urate*, $2C_5H_3O_3N_4Na,H_2O$. *Normal lithium urate* is moderately soluble in water.

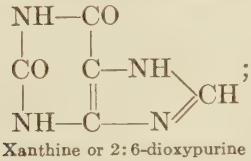
Uric acid is present in urine, an adult producing about one gramme in twenty-four hours. It is the principal constituent of the excrement of birds, reptiles, and serpents; and can be prepared conveniently from serpent-excrement, which contains about 90 per cent. of the acid. In certain pathological diseases of the human organism such as gout, uric acid is deposited in the joints in the form of sparingly soluble primary salts. On account of the solubility of lithium urate, lithium hydroxide is prescribed as a remedy.

272. Compounds with the same carbon-nucleus as uric acid occur in nature, partly in the animal world and partly in the vegetable kingdom. Among the animal products are *hypoxanthine*, $C_5H_4ON_4$; *xanthine*, $C_5H_4O_2N_4$; and *guanine*, $C_5H_5ON_5$. The second class includes the vegetable bases *theobromine*, $C_7H_8O_2N_4$; and *caffeine*, $C_8H_{10}O_2N_4$. To rationalize the nomenclature of these substances

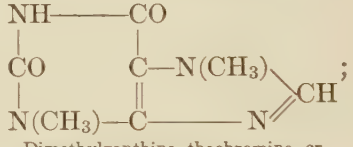
and that of other members of the group, Emil Fischer regarded them as derivatives of *purine* (273), its carbon atoms and nitrogen atoms being numbered as indicated in the formula



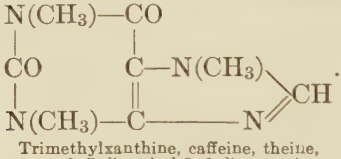
Xanthine, theobromine, and caffeine have the following structural formulæ and rational names:



Xanthine or 2:6-dioxypurine



Dimethylxanthine, theobromine, or 3:7-dimethyl-2:6-dioxypurine



Trimethylxanthine, caffeine, theine, or 1:3:7-dimethyl-2:6-dioxypurine

Theobromine and caffeine are formed by the introduction of methyl-groups into xanthine.

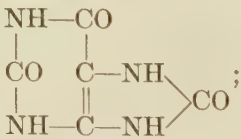
Xanthine, $C_5H_4O_2N_4$, is present in all the tissues of the human body. It is a colourless powder, soluble with difficulty in water, and possessing a weak basic character. Its oxidation yields alloxan and urea.

Theobromine, $C_7H_8O_2N_4$, is prepared from cocoa. It is only slightly soluble in water, and is converted by oxidation into *monomethylalloxan* and *monomethylurea*.

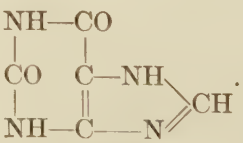
Caffeine or *theine*, $C_8H_{10}O_2N_4$, is a constituent of coffee and tea. It crystallizes with one molecule of water in long silky needles, and is moderately soluble in water. Usually it is prepared from tea-dust. Its careful oxidation yields *dimethylalloxan* and *monomethylurea*.

The position of the methyl-groups in theobromine and caffeine is indicated by the formation of these oxidation-products.

There is an evident resemblance between the constitution of uric acid and that of xanthine:



Uric acid

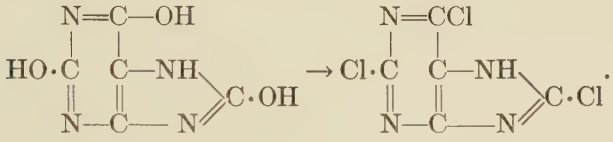


Xanthine

These formulæ indicate the possibility of obtaining xanthine by the reduction of uric acid, and up to the year 1897 numerous unsuccessful attempts were made to prepare it by this method, a reaction ultimately effected by Emil Fischer in that year. He discovered several methods of converting uric acid into xanthine and its methyl-derivatives, including one now available for the manufacture of the therapeutically important bases theobromine and caffeine.

273. Direct replacement of oxygen in uric acid by hydrogen does not seem possible, but Emil Fischer substituted chlorine for oxygen by means of phosphorus oxychloride. Various methods of replacing the chlorine atoms in these halogen derivatives by other groups or atoms have been devised.

When uric acid reacts with phosphorus oxychloride, the first product is 8-*oxy*-2:6-*dichloropurine*. Further careful treatment with the same reagent converts this substance into 2:6:8-*trichloropurine*:



Tautomeric form of uric acid

2:6:8-Trichloropurine

The behaviour of uric acid in this reaction accords with the tautomeric (**235**) formula of trihydroxypurine, the phosphorus oxychloride replacing the hydroxyl-groups with chlorine atoms in a normal manner.

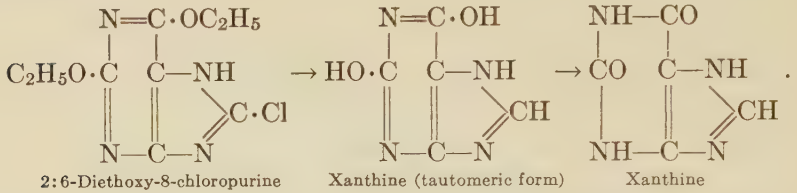
At 0° in presence of hydrogen iodide and phosphonium iodide, trichloropurine changes into *di-iodopurine*:

$$C_5HN_4Cl_3+4HI=C_5H_2N_4I_2+3HCl+2I.$$

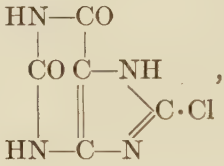
Reduction of the aqueous solution of di-iodopurine with zinc-dust yields *purine*, a white crystalline substance melting at 216°-217°, and very readily soluble in water. It has a weak basic character, but does not turn red litmus blue.

Xanthine is obtained from trichloropurine by the following process. Chlorine atom 8 in this compound is very stable towards alkalis, whereas chlorine atoms 2 and 6 are displaced with comparative ease. Trichloropurine reacts with sodium ethoxide, replacing chlorine atoms 2 and 6 by ethoxyl-groups. Heating the compound obtained with a solution of hydrogen iodide replaces the ethyl-groups by hydrogen,

chlorine atom 8 being exchanged simultaneously for a hydrogen atom, with formation of xanthine:



When 2:6-*diethoxy*-8-*chloropurine* is heated with hydrochloric acid, only the ethyl-groups are replaced by hydrogen, with production of a compound of the formula



the tautomeric enolic form changing to the ketonic modification. On methylating this substance, its three hydrogen atoms are exchanged for methyl-groups, yielding *chlorocaffeine*, a substance convertible by nascent hydrogen into caffeine. The process affords a means of preparing caffeine from uric acid.

Emil Fischer discovered a very characteristic and simple mode of effecting this methylation. It involves agitation of an alkaline aqueous solution of uric acid with methyl iodide, the four hydrogen atoms being replaced by methyl-groups and a *tetramethyluric acid* formed. With phosphorus oxychloride, $POCl_3$, this derivative yields chlorocaffeine:

$$3C_5O_3N_4(CH_3)_4+POCl_3=3C_5O_2N_4(CH_3)_3Cl+PO(OCH_3)_3.$$

Chlorocaffeine can be converted by nascent hydrogen into caffeine.

SECOND PART.

CYCLIC COMPOUNDS.

INTRODUCTION.

274. With only few exceptions, the compounds described in the first part of this book contain an open chain. Examples of these exceptions are *cyclic* compounds such as the lactones, the anhydrides of dibasic acids, and the uric-acid group. The *closed chain* of such compounds becomes opened very readily, and the close relationship of their methods of formation and properties with those of the open-chain derivatives makes it desirable to include them in a description of the aliphatic compounds.

There exists a large number of substances containing closed chains of great stability towards every kind of chemical reagent, and with properties differing in many important respects from those of the aliphatic compounds. They are termed *cyclic compounds*, and are classified as follows:

A. Carbocyclic compounds, with a closed ring of carbon atoms only, subdivided into

1. *Alicyclic compounds*, such as the *cyclo*paraffin derivatives or cyclanes (**121**), and

2. *Aromatic compounds*, or benzene derivatives. In this class are included the compounds with *condensed rings*, or two closed chains with atoms common to each. The typical representative of this type of condensed ring is *naphthalene*, $C_{10}H_8$, with two benzene-nuclei.

B. Heterocyclic compounds, with rings containing carbon atoms and one or more atoms of another element. This class is exemplified by *pyridine*, C_5H_5N, and its derivatives, with a ring of five carbon atoms and one nitrogen atom; *furan*, C_4H_4O, with four carbon atoms and one oxygen atom; *pyrrole*, C_4H_5N, with four carbon atoms and one nitrogen atom; *thiophen*, C_4H_4S, with four carbon atoms and one sulphur atom; *pyrazole*, $C_3H_4N_2$, with three carbon atoms and two nitrogen atoms; and numerous other combinations.

Two dissimilar rings also can have atoms in common, as in *quinoline*, C_9H_7N, with a benzene-nucleus and a pyridine-nucleus.

Numerous derivatives of all these compounds being known, the scope of the cyclic division of organic chemistry is much more extended than that of the aliphatic division.* The description of the cyclic group is, however, simplified greatly by the recurrence of the properties of alcohols, aldehydes, acids, etc., already described for the aliphatic compounds.

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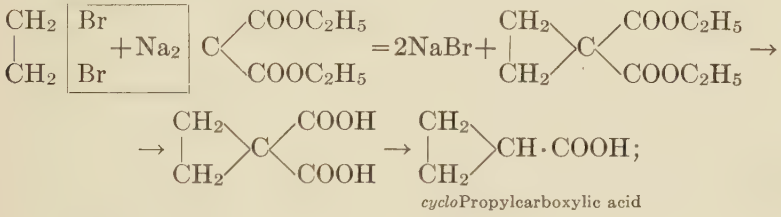
* Its wide range is indicated by the fact that about 400 ring-systems have been described.

A. CARBOCYCLIC COMPOUNDS.

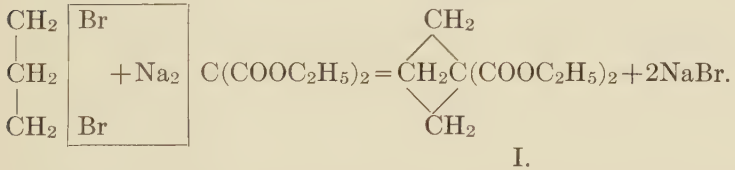
1. ALICYCLIC COMPOUNDS.

275. The most important methods for the preparation of *alicyclic compounds* will be indicated.

The first method consists in the interaction of dibromoalkanes with terminal bromine atoms and diethyl disodiomalonate to yield cyclo*propane derivatives* and cyclo*butane derivatives:*



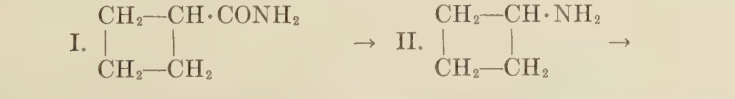
*cyclo*Propylcarboxylic acid



I.

From each molecule of the dibasic acid obtained by the saponification of the ester marked I heat expels one molecule of carbon dioxide (**164**), yielding cyclo*butylcarboxylic acid.*

276. cyclo*Butane* is formed from this acid by a method applicable to the preparation of other hydrocarbons. The acid amide (I) is converted by the method of **259** into cyclo*butylamine* (II). With excess of methyl iodide this amine yields the iodide of the quaternary ammonium base III, a substance convertible into the free base. Dry distillation decomposes it (**66**) into trimethylamine, water, and *cyclo*butene (IV):



Careful reduction with hydrogen and nickel converts *cyclo*butene into *cyclo*butane.

The main product of the oxidation of cyclo*butanol*, $\begin{matrix}CH_2—CHOH\\ |\quad\quad |\\ CH_2—CH_2\end{matrix}$, is cyclo*propanal*, $\begin{matrix}CH_2\\ |\quad\diagdown\\ |\quad CH\cdot C\overset{H}{\underset{O}{}}\\ |\quad\diagup\\ CH_2\end{matrix}$, cyclo*butanone* also being formed.

This reaction is remarkable as an illustration of the transformation of a ring of four carbon atoms into one of three carbon atoms. The converse change of a *cyclo*butyl-ring to a *cyclo*pentyl-ring is exemplified by digesting cyclo*butylcarbinol*, $\begin{matrix}CH_2—CH\cdot CH_2OH\\ |\quad\quad |\\ CH_2—CH_2\end{matrix}$, with concentrated hydrogen bromide, the corresponding bromide being formed. This halide is transformed by nascent hydrogen into *cyclo*pentane, instead of *methyl*cyclo*butane*.

277. The second method of preparing alicyclic compounds furnishes a very general means for the production of cyclo*alkanones*. It involves the dry distillation of salts of the dibasic acids with terminal carboxyl-groups. The process renders possible the formation of ring-systems having between five and twenty-nine carbon atoms in a closed chain. By this reaction calcium adipate or butanedicarboxylate yields cyclo*pentanone:*

$$\begin{matrix}CH_2\cdot CH_2\cdot CO\cdot O\\ |\quad\quad\quad\quad\diagdown\\ CH_2\cdot CH_2\cdot CO\ O\end{matrix}\!\!>\!Ca = CaCO_3 + \begin{matrix}CH_2\cdot CH_2\\ |\quad\quad\diagdown\\ CH_2\cdot CH_2\end{matrix}\!\!>\!CO.$$

Calcium adipate — *cyclo*Pentanone

Formerly calcium salts only were employed for this purpose, but the yields of the higher derivatives from cyclo*nononanone* onwards were very poor. By substituting thorium salts Ruzicka has been able to obtain satisfactory yields of the *cyclo*ketones.

The structure of *cyclo*pentanone is indicated by its oxidation to glutaric acid:

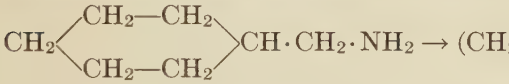
$$\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad\diagdown\\ CH_2\cdot CH_2\end{matrix}\!\!>\!CO \rightarrow \begin{matrix}CH_2\cdot CH_2\cdot COOH\\ |\\ CH_2\cdot COOH\end{matrix}.$$

Glutaric acid

This reaction presents a contrast to the oxidation of a straight-chain ketone to two acids. The possibility of the compound being an aldehyde is excluded by the failure to oxidize it to a monobasic acid with the same number of carbon atoms.

*cyclo*Pentanone is a liquid of peppermint-like odour, but the higher members of the series are solids resembling camphor in appearance. Those having a ring of between fourteen and eighteen carbon atoms are characterized by an odour of musk; and RUZICKA has isolated from civet cyclo*decenone*, $C_{17}H_{30}O$, an unsaturated *cyclo*ketone. On addition of two hydrogen atoms it becomes identical with cyclo*heptadecanone*, a *cyclo*ketone obtained by dry distillation of thorium hexadecanedicarboxylate-1 : 16. The odoriferous principle of musk is named *muscone*. It is optically active, and its structure is 1-*methyl*-cyclo*pentadecane*-3-*one*.

278. A third method of preparing alicyclic compounds is that of DEMJANOV, whereby a compound of this type can be converted into another with an additional carbon atom. The process can be exemplified by the transformation of *cyclo*hexylmethylamine (I), a substance characterized by the remarkable property of yielding a stable nitrite (II):



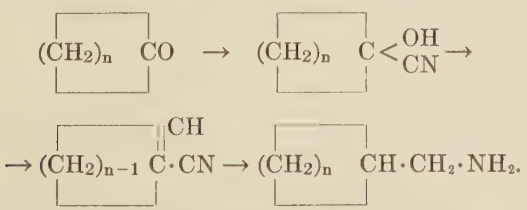
I. II.

Boiling in acetic-acid solution eliminates nitrogen and water and transforms these nitrites into the alcohols of the next higher ring-system:

$$(CH_2)_5{>}CH\cdot CH_2\cdot NH_2\cdot NO_2H \rightarrow (CH_2)_6{>}CHOH.$$

The conversion into suberone by oxidation of the alcohol formed from *cyclo*hexylmethylamine demonstrates the course of this reaction. By these means it is possible to ascend from *cyclo*propane derivatives to *cyclo*octane derivatives.

The first step in the preparation of the amines required for this process is the addition of an equimolecular proportion of hydrogen cyanide to a *cyclo*alkanone. Thionyl chloride, $SOCl_2$, eliminates water from the hydroxycarbonitrile formed, yielding an unsaturated *cyclo*carbonitrile. Nascent hydrogen adds two hydrogen atoms at the double bond, simultaneously changing the cyano-group to a CH_2NH_2-group:



279. The cyclic hydrocarbons, C_nH_{2n}, from cyclo*propane* to cyclo*octane* have been isolated. The table contains a comparison of some of their

physical constants with the corresponding constants of the normal hydrocarbons of the saturated series C_nH_{2n+2}, and with those of the unsaturated series, C_nH_{2n}.

Number of Carbon Atoms.	C_nH_{2n+2}.		C_nH_{2n}, Unsaturated.		C_nH_{2n}, Cyclic.	
	Boiling-point.	Density.	Boiling-point.	Density.	Boiling-point.	Density. D_4^0.
3	−45°	0·536 (0°)	− 48·2°		*ca.*−35°	
4	1°	0·600 (0°)	− 5°		11°–12°	0·7038
5	36·3°	0·627 (14°)	35°	0·648 (0°)	49°	0·7635
6	68·9°	0·658 (20°)	68°	0·683 (15°)	81°	0·7934
7	98·4°	0·683 (20°)	98°	0·703 (19·5°)	117°	0·8252
8	125·6°	0·702 (20°)	124°	0·722 (17°)	147°	0·850

The saturated cyclic hydrocarbons have higher boiling-points and much higher densities (about 0·12) than their unsaturated isomerides. The saturated hydrocarbons contain two hydrogen atoms more than the corresponding alkenes. The members of these two series with the same number of carbon atoms have almost the same boiling-points, but their densities are about 0·02 lower.

The molecular volumes of the unsaturated compounds are appreciably higher than those of the corresponding isomeric cyclic derivatives. For hexene the molecular volume is 123·0, and for *cyclo*hexane 106·4. The presence of a double bond obviously augments the volume considerably.

280. Ring-systems with three to five carbon atoms are under positive strain, the angle between two affinity-directions being smaller than that normal for a carbon atom not in cyclic combination (**167**). As a consequence all the carbon atoms of such systems can be situated in the same plane. For a ring-system containing six or more carbon atoms lying in the same plane the strain is negative, the angle being greater than the normal. Whilst the positive strain of ring-systems with three to five carbon atoms keeps these atoms in the same plane, the negative strain of larger ring-systems tends to induce distortion of the polygon, the position of all carbon atoms in the same plane being unstable.

By assuming not all the carbon atoms to be situated in the same plane, it is possible to visualize for such ring-systems polygons free from strain.

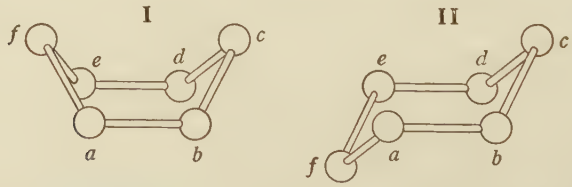


FIG. 66.—EXAMPLES OF SACHSE'S MODELS FOR *cyclo*HEXANE.

It is years since Sachse constructed for *cyclo*hexane strainless models exemplified in Fig. 66.

The impossibility of assuming all the carbon atoms to lie in the same plane applies equally to Ruzicka's *cyclo*ketones with ring-systems up to thirty carbon atoms. Such an arrangement would render the systems very unstable, whereas he demonstrated them to be characterized by great stability. This property is exemplified by the capacity of the higher cyclanes to withstand heating with concentrated hydrogen iodide at 250°, and by that of the *cyclo*ketones to resist hydrogen chloride at 190°, neither type of ring-system undergoing rupture. The assumption of this type of configuration would demand the possibility of each monosubstitution-product existing in two isomeric forms, as well as a much greater number of higher substitution-products than have been discovered, but this objection has been countered by a suggestion made by Mohr. According to his view these configurations should not be regarded as unchanging, but as continually undergoing transformation from one into another, the ring-system being in a *fluctuating condition*. An experimental proof in support of Mohr's theory is given in **364**.

In studying the refraction of the cyclanes and their derivatives, Eykman found the difference between their molecular refractions and those of the corresponding saturated compounds with the formula C_nH_{2n+2} not constant, but dependent on the number of carbon atoms in the nucleus, and also on the presence or absence of side-chains. The smaller the number of carbon atoms in the nucleus, the greater is the molecular refraction of isomerides, and its value is still higher in substances with a double bond. The most probable explanation of this phenomenon is the strain characteristic of these ring-systems (**120**). The double linking involves the greatest strain, the carbon bonds being deflected from the normal position to the extent of 54° 41′. For a ring of three carbon atoms the deflection is 24° 44′, for a ring of four carbon atoms 9° 34′, and for a ring of five carbon atoms only a few minutes.

The refraction method affords a valuable aid in ascertaining the nature of the ring-systems present in compounds.

2. AROMATIC COMPOUNDS.

General Properties.

281. Certain substances found in the vegetable kingdom are characterized by the possession of an agreeable aroma, examples being *oil of bitter almonds*, *oil of caraway*, *oil of cumin*, *balsam of Tolu*, *gum-benzoin*, and *vanilla*. These vegetable-products consist principally of substances of somewhat similar character, but differing from the aliphatic compounds in containing much less hydrogen in proportion to the other elements. This divergence is illustrated by *cymene*, $C_{10}H_{14}$, from oil of caraway; *toluene*, C_7H_8, from balsam of Tolu; and *benzoic acid*, $C_7H_6O_2$, from gum-benzoin. The corresponding saturated aliphatic compounds with the same number of carbon atoms have the formulæ $C_{10}H_{22}$, C_7H_{16}, and $C_7H_{14}O_2$.

Before the nature of the so-called *aromatic* compounds had been closely investigated, it was customary on account of their external similarity to regard them as members of a single group, just as ordinary butter and "butter of antimony," $SbCl_3$, were classed together because of their similarity in consistence. This method of classification is still adopted for compounds with analogous properties, but of imperfectly understood constitution, such as the bitter principles, some vegetable alkaloids, and many vegetable dyes.

A closer study of the aromatic compounds has revealed the old and somewhat arbitrary classification according to external resemblance to be well founded, for all these substances can be considered derivatives of one hydrocarbon, *benzene*, C_6H_6, just as the aliphatic compounds can be regarded as derived from methane, CH_4. An example is the oxidation of toluene to benzoic acid, and the conversion of its calcium salt into benzene by distillation with lime. The dibasic terephthalic acid, $C_8H_6O_4$, is formed by the oxidation of cymene, and can be transformed similarly into benzene.

The derivatives of benzene are therefore known as *aromatic compounds*. In addition to the property of being convertible into benzene, they possess certain other noteworthy characteristics, the more important being described in the next section.

282. The saturated hydrocarbons of the aliphatic series are not attacked by concentrated nitric acid or sulphuric acid, and only to a small extent by oxidizers, but their halogen-substituted derivatives react with great ease. The aromatic hydrocarbons differ from the aliphatic hydrocarbons in all these respects.

1. The aromatic hydrocarbons are attacked readily by concentrated nitric acid, with formation of *nitro-compounds*:

$$C_6H_5\cdot\boxed{H+HO}\cdot NO_2 = \underset{\text{Nitrobenzene}}{C_6H_5\cdot NO_2} + H_2O.$$

These substances reduce to amino-derivatives, and consequently are true nitro-compounds.

2. With concentrated sulphuric acid the aromatic compounds yield *sulphonic acids*:

$$C_6H_5\cdot\boxed{H+HO}\cdot SO_3H = \underset{\text{Benzenesulphonic acid}}{C_6H_5\cdot SO_3H} + H_2O.$$

The sulphur of the sulpho-group is united with a carbon atom of the benzene-nucleus, for thiophenol, $C_6H_5\cdot SH$, also oxidizes to benzenesulphonic acid:

$$C_6H_5\cdot SH \rightarrow C_6H_5\cdot SO_3H.$$

3. The aromatic hydrocarbons with side-chains are oxidized without difficulty to acids, the whole side-chain usually being eliminated as far as the carbon atom in union with the nucleus, with formation of carboxyl.

4. Chlorobenzene and bromobenzene have their halogen atoms so firmly attached to the phenyl-group, C_6H_5, as almost to be incapable of taking part in double decompositions with such compounds as metallic alkoxides, salts, and so on.

Syntheses from Aliphatic Compounds.

Certain syntheses of aromatic substances from aliphatic compounds are cited here, and other examples are given in the chapter on hydrocyclic derivatives (**363** and **364**).

1. When the vapours of volatile aliphatic compounds are passed through a red-hot tube, aromatic substances are among the products. The condensation of acetylene, C_2H_2, to benzene is a typical example, although passage through a red-hot tube transforms benzene-vapour into acetylene, proving both reactions to be incomplete. Besides

benzene, other aromatic compounds also are formed. A synthesis of benzene from carbon monoxide is described in **337**.

2. Sulphuric acid converts acetone into *mesitylene*, or 1:3:5-trimethylbenzene (**285**):

$$3C_3H_6O - 3H_2O = C_9H_{12}.$$

Other ketones condense similarly to aromatic hydrocarbons.

3. This type of reaction is exemplified further by the syntheses of *cyclo*hexane, phloroglucinol, and mellitic acid.

BENZENE AND THE AROMATIC HYDROCARBONS WITH SATURATED SIDE-CHAINS.

Gas-manufacture and its By-products: Tar.

283. The aromatic hydrocarbons are obtained technically by the dry distillation of coal in retorts raised to a red heat. The products are *gas*, employed for lighting and heating; *tar*, containing the hydrocarbons; and *coke*, remaining in the retorts.

In recent years important investigations as to the composition of coal have been made, and have proved it to consist mainly of black masses of substances with the humus character, produced by the decay of the remains of plants containing cellulose. There are also present resinous bodies extractible by pyridine and other solvents, the process of dry distillation converting these products into tar.

The composition of the *vacuum-tar* obtained by the distillation of coal *in vacuo* is quite different from that of the tar produced at ordinary pressure, for it contains a very small proportion of aromatic hydrocarbons and a large proportion of both saturated and unsaturated *cyclo*paraffins. When passed through a red-hot tube filled with coke, these paraffins yield a tar in all respects similar to that produced in gas-manufacture. The process probably involves two stages:

1. At a low temperature the resinous constituents of the coal decompose, forming *cyclo*hydrocarbons;

2. At a higher temperature these hydrocarbons undergo transformation into gas and ordinary tar.

Tar is a thick black liquid with a characteristic odour. Its colour is due to suspended particles of carbon. It is a complex mixture of neutral, acidic, and basic substances. The first are principally hydrocarbons, chiefly belonging to the aromatic series. Between 5 and 10 per cent. of the tar consists of naphthalene, and between 1 and 1·5 per cent. of a mixture of benzene and toluene. Phenol (**294**) is the principal acidic constituent of tar. Basic substances are present only in small proportion, the chief being pyridine, quinoline, and their homologues.

The technical separation of the tar-products is effected partly by chemical means, and partly by fractionation. The first operation is to

distil the tar, a considerable proportion remaining in the retort as a black, either soft or somewhat brittle mass, known as *pitch*. The distillate is submitted to fractional distillation, four fractions being obtained:

1. Light oil, between 80° and 170° with a density from 0·910 to 0·950.

2. Middle oil, or carbolic oil, between 170° and 230°, with the density 1·01.

3. Heavy oil, or creosote-oil, between 230° and 270°, with the density 1·04.

4. Green oil or anthracene-oil, above 270°, with the density 1·10.

The light oil contains benzene and its homologues, these substances being separable by further fractionation. Only a limited number of the homologues of benzene is present in the light oil. They consist principally of *toluene* or methylbenzene, and *xylene* or dimethylbenzene.

Benzene and its Homologues.

284. The homologues of benzene can be prepared by the method of Wurtz-Fittig, and by that of Friedel and Crafts.

1. The Wurtz-Fittig synthesis involves the interaction of either bromobenzene, or in general a hydrocarbon with bromine in the nucleus, and an alkyl bromide or iodide in presence of sodium (**29**):

$$\begin{matrix} C_6H_5 \\ + \end{matrix}\boxed{\begin{matrix} Br + Br \\ Na \quad Na \end{matrix}}\begin{matrix} C_2H_5 \\ \end{matrix} = \underset{\text{Ethylbenzene}}{C_6H_5—C_2H_5} + 2NaBr.$$

Sometimes a series of by-products is obtained, among them paraffins and diphenyl, $C_6H_5 \cdot C_6H_5$. With the higher normal primary alkyl iodides the yield of alkylbenzene is very good.

2. Friedel and Crafts's synthesis is peculiar to the aromatic series, and depends on a remarkable property of aluminum chloride. This substance is obtained by the action of dry hydrogen chloride on aluminium-foil. On bringing it into contact with a mixture of an aromatic hydrocarbon and an alkyl chloride, clouds of hydrogen chloride are evolved, and hydrogen of the nucleus is exchanged for the alkyl-group:

$$C_6H_5 \cdot \boxed{H + Cl}\, CH_3 = C_6H_5 \cdot CH_3 + HCl.$$

Usually in the synthesis of Friedel and Crafts more than one alkyl-group is introduced, the monosubstitution-products and the higher substitution-products being formed simultaneously. The mixture can be separated by fractional distillation.

This reaction constitutes a method both for the building-up and breaking-down of a hydrocarbon. Toluene, $C_6H_5 \cdot CH_3$, reacts with aluminium chloride to yield benzene, C_6H_6, and xylene, $C_6H_4(CH_3)_2$. The alkyl-groups of one hydrocarbon are exchanged for the hydrogen of the other. The transformation can be effected also by the action of concentrated sulphuric acid on aromatic hydrocarbons with a number of side-chains.

There are many different types of the reaction of Friedel and Crafts, and there has been much diversity of opinion as to its mechanism. Sometimes only a very small proportion of aluminium chloride suffices; in other reactions there must be at least one molecule of the chloride for each molecule of the reacting substance. Böeseken regards the process as one of simple catalysis, having proved reactions requiring a large excess of aluminium chloride to be attended by a combination between it and the other reacting substances, most of the aluminium chloride being rendered unreactive by the union.

3. By heating an alcohol, an aromatic hydrocarbon, and zinc chloride at temperatures between 270° and 300°. The zinc chloride acts as a dehydrator:

$$C_6H_5|\underline{H+HO}|\cdot C_5H_{11} = C_6H_5 \cdot C_5H_{11} + H_2O.$$

The following reactions also are available for the preparation of both benzene and its homologues:

4. Like the saturated aliphatic hydrocarbons, the aromatic hydrocarbons are obtained by the distillation with soda-lime of the calcium salts of the aromatic acids (83):

$$C_6H_5 \cdot \boxed{CO_2ca^* + caO}\, H = C_6H_6 + CaCO_3.$$

5. Benzene and its homologues can be obtained by heating the sulphonic acids with sulphuric acid or hydrochloric acid, the decomposition being facilitated by the introduction of superheated steam:

$$C_6H_3(CH_3)_2\boxed{SO_3H+HO}\,H = C_6H_4(CH_3)_2 + H_2SO_4.$$

This method can be employed in the separation of the aromatic hydrocarbons from the paraffins. Warming with concentrated sulphuric acid

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* $ca = \frac{1}{2}Ca$.

converts the aromatic derivatives into sulphonic acids soluble in water, the paraffins being unaffected and insoluble in water. By this means a mechanical separation is possible.

This method can be applied also to the separation of the aromatic hydrocarbons from one another, some of them being converted into sulphonic acids more readily than others.

285. Benzene and the aromatic hydrocarbons with saturated side-chains are colourless highly refractive substances, liquid at the ordinary temperature, and possessing a characteristic odour. They are immiscible with water, but mix in all proportions with strong alcohol. Some of their physical properties are indicated in the table:

Name.	Formula.	Boiling-point.	Density.
Benzene	C_6H_6	80·4°	0·874 (20°)
Toluene	$C_6H_5 \cdot CH_3$	110°	0·869 (16°)
m-Xylene	$C_6H_4 < \begin{matrix} CH_3\ 1 \\ CH_3\ 3 \end{matrix}$	139°	0·881 (0°)
Mesitylene	$C_6H_3(CH_3)_3$ (1:3:5)	164°	0·865 (14°)
Ethylbenzene	$C_6H_5 \cdot C_2H_5$	136°	0·883 (0°)
*iso*Propylbenzene (Cumene)	$C_6H_5 \cdot CH(CH_3)_2$	153°	0·866 (16°)
p-Methyl*iso*propylbenzene (Cymene)	$C_6H_4 < \begin{matrix} CH_3\ 1 \\ CH(CH_3)_2\ 4 \end{matrix}$	175°	0·856 (20°)

Usually the boiling-points of the isomeric benzene derivatives are very close together, but the melting-points display wide divergences. It is an almost invariable rule throughout the entire aromatic series for the *para*-compound to have a higher melting-point than the *meta*-compound and the *ortho*-compound.

Benzene was discovered by Faraday in 1825 in a liquid obtained from compressed coal-gas. Its solid form melts at 5·4°.

Xylene, or dimethylbenzene, exists in three isomeric forms. m-*Xylene* is the principal isomeride in tar, constituting between 70 and 85 per cent. of the xylenes present.

The isomeric xylenes are separable with difficulty, for their boiling-points lie very close together. That of *o*-xylene is 142°, while *m*-xylene boils at 139°, and *p*-xylene at 138°. This similarity makes their separation by fractional distillation impracticable, but it can be effected by sulphuric acid at the ordinary temperature. *m*-Xylene and *o*-xylene dissolve as sulphonic acids, *p*-xylene remaining undissolved. The sulphonic acid of the *meta*-compound and that of the *ortho*-compound can be separated by fractional crystallization of their sodium salts, the *ortho*-salt crystallizing first.

Cymene, $C_{10}H_{14}$, is related closely to the terpenes $C_{10}H_{16}$, and to the camphors $C_{10}H_{16}O$, for it can be obtained from them. Cymene is a constituent of certain essential oils, such as *oil of caraway*, *oil of thyme*, and *oil of eucalyptus*. It is obtained in large quantities from the terpenes present in the coniferous woods employed for the production of cellulose (**228**) by the sulphite-process.

Constitution of Benzene.

286. As stated in **281**, all the aromatic compounds are convertible into benzene. The discovery of this relationship by KEKULÉ brought into prominence the question of its constitution. Its formula, C_6H_6, contains eight hydrogen atoms less than that of the saturated paraffin with six carbon atoms, hexane, C_6H_{14}. Benzene, like other hydrocarbons poor in hydrogen, such as C_6H_{12} and C_6H_{10}, might be supposed to contain multiple carbon bonds, but its properties do not admit of this assumption. Compounds with a multiple carbon bond readily form addition-products with the halogens, are very sensitive to oxidizers, and react easily with VON BAEYER'S reagent (**113**); but benzene lacks these properties. It yields halogen addition-products very slowly, whereas compounds with a multiple carbon bond form them instantaneously. Benzene therefore cannot contain multiple carbon bonds, and the carbon atoms in its molecule must be united in a special manner.

Comprehension of the mode of union of the benzene carbon atoms involves a knowledge of the relative distribution of its hydrogen and carbon atoms. Two facts suffice to determine it. First, *isomerides of the monosubstitution-products of benzene are unknown*. Second, *the disubstitution-products exist in three isomeric forms*. Accordingly, there is only one monobromobenzene, C_6H_5Br; but three dibromobenzenes are known, distinguished by the prefixes *ortho*, *meta*, and *para*.

The equivalence of the six hydrogen atoms of benzene (**359**) follows from the first of these facts, replacement of any one of them yielding the same monosubstitution-product. Three formulæ with the six hydrogen atoms of equal value are possible for benzene:

$$\text{I. } C_4(CH_3)_2; \quad \text{II. } C_3(CH_2)_3; \quad \text{III. } (CH)_6.$$

The degree of accord of each of these formulæ with the second fact demands consideration.

A disubstitution-product of a compound with formula I can be either

$$C_4\begin{cases}CH_2X\\CH_2X\end{cases} \quad \text{or} \quad C_4\begin{cases}CHX_2\\CH_3\end{cases}.$$

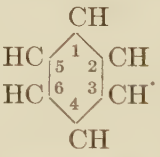
Other isomerides being impossible, this formula is inadmissible, for it leads to two isomerides instead of to three.

With formula II four isomerides seem possible:

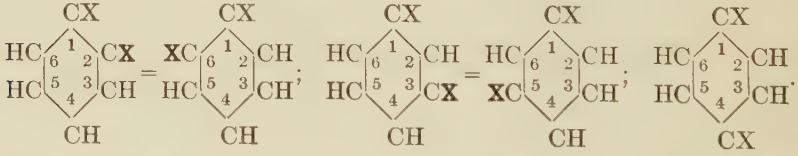
$$a.\ C_3\begin{cases}CHX\\CHX,\\CH_2\end{cases}\qquad b.\ C_3\begin{cases}CHX\\CH_2\ ,\\CHX\end{cases}\qquad c.\ C_3\begin{cases}CX_2\\CH_2,\\CH_2\end{cases}\qquad d.\ C_3\begin{cases}CH_2\\CX_2.\\CH_2\end{cases}$$

The hydrogen atoms in benzene being equivalent, the CH_2-groups in the benzene molecule must be united similarly, *a* being equal to *b*, and *c* to *d*. In consequence the number of possible isomerides is reduced to two. Formula II cannot be accepted either, for it also fails to explain the formation of three isomeric disubstitution-products.

There remains only formula III with each carbon atom in union with one hydrogen atom. The question of the constitution of benzene therefore is narrowed to this problem: given a compound C_6H_6 having each carbon atom united with one hydrogen atom, the objective is to find a formula accounting for the equivalence of all the hydrogen atoms, the formation of three disubstitution-products, and the absence of double or multiple bonds. Evidently an open carbon-chain formula cannot fulfil the prescribed conditions, for the hydrogen atoms attached to such a chain containing terminal and intermediate CH-groups could not be equivalent. The six hydrogen atoms can be of equal value only in a ring of six carbon atoms:



This arrangement of the CH-groups also fulfils the second condition, as is evident from the scheme



In it the compounds $C_6H_4X_2$, with substituents at 1:2=1:6, 1:3=1:5, and 1:4, are isomeric. The formation of three isomerides therefore also becomes clear.

287. This hexagonal formula finds support in the evidence afforded by very many investigations of isomeric benzene derivatives, and

affords a partial elucidation of the constitution of benzene. Despite exhaustive investigation by the most eminent chemists, an entirely satisfactory explanation of the inner structure of the benzene molecule and of the mode of union of the fourth bond of each of the six carbon atoms is still lacking.

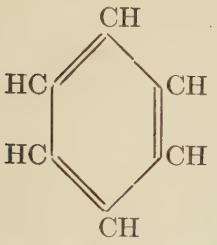


FIG. 67.—KEKULÉ'S BENZENE-FORMULA.

KEKULÉ assumed the presence of three double bonds in the benzene molecule, as indicated in Fig. 67.

There are two objections to KEKULÉ's formula, the first being the representation of benzene as an unsaturated compound. The second drawback is the dissimilarity of the two *ortho*-positions, the carbon atoms being united singly on one side, and doubly on the other.

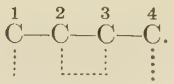
WILLSTÄTTER attempted the synthesis of the compound cyclo*hexatriene*, C_6H_6, with the constitution assigned by KEKULÉ to benzene. The starting point was cyclo*hexanol* (I), a substance converted readily into cyclo*hexene* (II) by elimination of water. A dibromide (III) was formed by addition of bromine, and one of its bromine atoms was eliminated as hydrogen bromide by the action of dimethylamine, the other bromine atom being replaced by the dimethylamino-residue (IV). The cyclo*hexylamine* formed reacted with methyl iodide and then with silver hydroxide, the product being a base (V), converted by dry distillation at reduced pressure (**276**) into cyclo*hexadiene* (VI). Compounds II and VI had all the properties characteristic of unsaturated derivatives. Addition of bromine to VI gave VII (compare **127** and below), a substance converted into the corresponding diammonium base by a process similar to that involved in the transformation of III into V. At the very low pressure of one-hundredth of a millimètre, this base was found to decompose at 0° into water, trimethylamine, and the compound with formula IX, a substance resembling benzene in all respects. The disappearance of the unsaturated character is an indication of the complete change in properties occasioned by the introduction of a third double bond into the ring of six carbon atoms.

The objections to KEKULÉ's formula have been met by a modification proposed by THIELE. He has made a special study of substances containing a conjugated linking (**127**), and has demonstrated such compounds to be converted into products with a double bond at the centre by addition of two univalent atoms:

$$—CH=CH—CH=CH— + 2X \rightarrow —CHX—CH=CH—CHX—.$$

CH2
CHOH
CH2
CH2
H2C
H2C
I.
CH
CH
II.
CHBr
CHBr
III.
CH—N(CH3)2
IV.
CH—N(CH3)3—OH
V.
VI.
CHBr
CHBr
VII.
CH—N(CH3)3—OH
VIII.
HC
HC
IX.

To explain this phenomenon, he assumed the whole of the affinity of the double bond not to be employed, a part termed the *residual affinity* remaining free at atoms 1 and 4, and the remainder being satisfied between atoms 2 and 3. This conception is indicated in the scheme



The dotted lines denote *partial valencies*. The hypothesis of valency-electrons (**244**) affords an insight into the possibility of the existence of such partial valencies. There is a double bond between carbon atoms 2 and 3, but it is *inactive*, for addition occurs only at 1 and 4.

The application of THIELE'S hypothesis to KEKULÉ'S formula gives a graphic representation (Fig. 68) with three inactive double bonds, but lacking free partial valencies. This peculiar type of structure might explain the difference between the properties of benzene and those of unsaturated compounds.

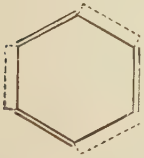


FIG. 68.—THIELE'S BENZENE-FORMULA.

By a method similar to that employed in his attempt to prepare *cyclo*hexatriene, WILLSTÄTTER synthesized cyclo*octatetraene* (Fig. 69). In accordance with THIELE'S hypothesis, this substance should possess only inactive double bonds, but the product was found to have the character of a highly unsaturated compound.

As a consequence of this fact it is necessary to assume the great stability to be due to the mutual affinities of the carbon atoms only for a ring of six such atoms with alternating single and double bonds; whilst for an analogous ring of eight atoms the increased distance between the carbon atoms constitutes a hindrance to stability, since the attracting forces diminish rapidly with increase in the distance between these atoms.

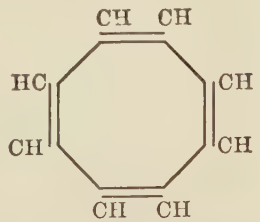


FIG. 69.—WILLSTÄTTER'S *cyclo*OCTATETRAENE.

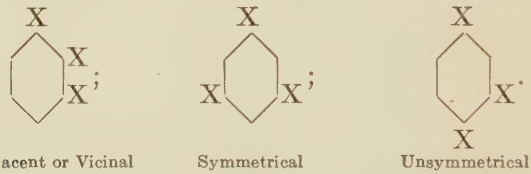
The spacial representation of the molecule of benzene must fulfil the condition of having the carbon atoms in the same plane as the hydrogen atoms. Any other type of spacial formula would indicate the possibility of optical isomerism for the disubstitution-products, and the existence of such a phenomenon lacks experimental foundation. THIELE'S modification of KEKULÉ'S formula fulfils this condition, and at present must be regarded as giving the best interpretation of the properties of benzene.

Nomenclature and Isomerism of the Benzene Derivatives.

288. The different isomeric disubstitution-products are distinguished by the prefixes *ortho*, *meta*, and *para*, or the positions of their substituents are denoted by numbers:

1:2=1:6 substitution-products are termed *ortho*-compounds.
1:3=1:5 " " " " *meta*-compounds.
1:4 " " " " *para*-compounds.

The number of isomeric substitution-products is the same for two similar or dissimilar substituents, but not for three. When the three groups are similar, three isomerides exist:



Adjacent or Vicinal 1:2:3 | Symmetrical 1:3:5 | Unsymmetrical 1:3:4

When one of the groups is dissimilar to the other two, different vicinal derivatives result by substitution at 2 and at 3 respectively; and, for the unsymmetrical compound, substitution at 3 produces a different compound from that formed by exchange at 4. For four similar groups the same number (three) of isomerides is possible as for two, since the two remaining hydrogen atoms can be in the *ortho*-position, *meta*-position, or *para*-position to one another. The number of isomerides possible in other cases can be determined readily.

An alkyl-radical or other group linked to a benzene-residue, as in $C_6H_5 \cdot CH_3$ or $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3$, is designated a *side-chain*, the benzene-residue being named the *nucleus*. Substitution is possible both in the nucleus and in the side-chain. With the first type of substitution it is usual to locate the *position* of the new substituent by reference to those already present, this process being termed the *determination of position*, or *orientation*, of the substituents. The methods of orientation are given in **354** to **358**.

MONOSUBSTITUTION-PRODUCTS OF THE AROMATIC HYDROCARBONS.

I. MONOHALOGEN COMPOUNDS.

289. Simple contact of the halogens with benzene does not produce substitution-products. Fluorine reacts with this hydrocarbon very energetically, decomposing the molecule completely, with formation of hydrogen fluoride and carbon tetrafluoride. Chlorine and bromine dissolve in benzene, and convert it slowly into the addition-products *hexachlorobenzene*, $C_6H_6Cl_6$, and *hexabromobenzene*, $C_6H_6Br_6$, both reactions being accelerated by sunlight. Iodine has no action, except at very high temperature. The substitution of hydrogen in benzene by chlorine or bromine can be effected only in presence of a catalyst, anhydrous ferric chloride or bromide being specially suitable. The process is exemplified by the preparation of *monobromobenzene*, C_6H_5Br, by the addition of bromine drop by drop to cooled dry benzene in presence of a small proportion of iron-powder. Ferric bromide is formed first, monobromobenzene being produced subsequently with evolution of hydrogen bromide. *Monoiodobenzene*, C_6H_5I, is prepared by heating benzene with iodine and iodic acid in a sealed tube, the iodic acid oxidizing to iodine and water the hydrogen iodide formed, and thus preventing it from reconverting the monoiodobenzene into benzene. Replacement by chlorine or bromine of the hydrogen of the nucleus in the homologues of benzene also necessitates the presence of a catalyst such as iron. Another method of preparing the halogen derivatives of benzene is described in **307**, 4.

The halogen atom in the monohalogen derivatives of benzene can be induced to react only with great difficulty. They can be boiled with alkali, with potassium hydrogen sulphide, with potassium cyanide, or can be heated with ammonia, without substitution of the halogen atom. The replacement of chlorine or bromine by the amino-group proceeds with tolerable smoothness, however, in presence of cupric sulphate, a reaction exemplified by the formation of aniline, $C_6H_5NH_2$, by heating monochlorobenzene with a concentrated aqueous solution of ammonia in presence of a small proportion of this salt in an autoclave at a temperature of about 180°. Replacement of halogen by the

methoxyl-group can be effected by the action at 220° of the powerful reagent sodium methoxide.

The character conferred on a halogen atom by union with the benzene-nucleus is completely analogous to that possessed by halogen attached to a doubly-linked carbon atom in an aliphatic unsaturated halogen derivative (**128**).

The WURTZ-FITTIG synthesis (**284**, 1) is one of the few examples of the ready displacement of a halogen atom in union with the benzene-nucleus. Magnesium reacts with an ethereal solution of monobromobenzene as with a similar solution of an alkyl halide (**75**). It yields a solution of a compound of the formula $C_6H_5 \cdot Mg \cdot Br$, a substance available for the synthesis of tertiary alcohols with the group C_6H_5, as described in **102**.

Monochlorobenzene is a colourless liquid boiling without decomposition at 132°, and with the density 1·106 at 20°. *Monobromobenzene* boils at 157°, and at 20° has the density 1·491. The boiling-point of *monoiodobenzene* is 188°, and at 0° the density is 1·861.

Iodobenzene and other iodine compounds substituted in the nucleus can add two atoms of chlorine, with formation of substances such as *phenyl-iodide chloride* or *iodobenzene dichloride*, $C_6H_5 \cdot ICl_2$. Digestion with alkalis converts these derivatives into *iodoso-compounds* such as *iodosobenzene*, $C_6H_5 \cdot IO$. These compounds are amorphous yellowish solids, and are transformed into *iodoxy-compounds* by heat and also by oxidation with bleaching-powder:

$$2C_6H_5 \cdot IO = C_6H_5 \cdot I + \underset{\text{Iodoxybenzene}}{C_6H_5 \cdot IO_2}.$$

Iodoxybenzene is crystalline, and is exploded by heat.

The constitution of these compounds is inferred from their ready conversion into iodobenzene, effected for iodosobenzene by means of potassium iodide, and for iodoxybenzene by hydrogen dioxide, with evolution of oxygen. These substances would not be converted into iodobenzene so readily if the oxygen were attached to the benzene-nucleus.

II. MONONITRO-DERIVATIVES.

290. A point of characteristic difference between the aromatic derivatives and the aliphatic compounds is the ready conversion of the aromatic substances into nitro-derivatives by the action of concentrated nitric acid (**282**, 1). This process is the only method employed in practice for the preparation of aromatic nitro-compounds. The substance is brought into contact with a mixture of nitric acid and sulphuric acid, or with excess of fuming nitric acid of density 1·52:

$$C_6H_5 \cdot \boxed{H + HO} \cdot NO_2 = C_6H_5 \cdot NO_2 + H_2O.$$

In the absence of the sulphuric acid or an excess of nitric acid, the water formed in the nitration would dilute the nitric acid and stop the action. This effect is explicable by assuming dilution to cause ionization of the nitric acid, the nitration-process requiring an unionized acid to ensure the presence of a hydroxyl-group capable of reacting with a hydrogen atom of the benzene to form water. Increase in the number of alkyl-groups attached to the benzene-nucleus often is accompanied by a corresponding increase in ease of nitration.

The mononitro-compounds are very stable, can be distilled without decomposition, and have their nitro-groups very firmly attached to the nucleus. Unlike the primary and secondary nitro-compounds of the aliphatic series, the aromatic nitro-derivatives do not contain hydrogen replaceable by metals, their nitro-group being united with a tertiary carbon atom. This fact inhibits such an exchange (**69**). Reduction of the nitro-compounds yields amines, the isolation of various intermediate products being made possible by modifying the course of the reaction (**296–304**).

Most of the mononitro-compounds have a pale-yellow colour and an agreeable odour. They are liquids insoluble in water, and are heavier than it. They are volatile with steam.

Nitrobenzene is manufactured in large quantities in the coal-tar dyestuff industry, cast-iron vessels with a stirrer and water-cooling being employed. They are charged with benzene, and into it a mixture of nitric acid and sulphuric acid is allowed to flow. At the end of the reaction, the sulphuric acid contains only a small proportion of nitric acid, and the nitrobenzene floating on its surface is washed with water and purified by distillation with steam.

Nitrobenzene is a yellowish liquid with an odour resembling that of bitter almonds, and is employed in perfumery. Its boiling-point is 208°, its melting-point 5·5°, and at 25° its density is 1·1987. It is poisonous, inhalation of its vapour being specially dangerous. It is prepared on a large scale to obtain *aniline* by its reduction (**297** and **303**).

Nitrotoluenes.—The chief products of the nitration of toluene are the *ortho*-compound and *para*-compound, only a small percentage of the *meta*-compound being formed. The proportion of *ortho*-derivative is greater than that of the *para*-isomeride, as is exemplified by the percentage-yields obtained by nitration at 0°, 58·8 of o-*nitrotoluene*, 36·8 of p-*nitrotoluene*, and 4·4 of m-*nitrotoluene*. Usually in simultaneous production of *ortho*-compounds and *para*-compounds, the *para*-isomeride is formed in greater proportion. *o*-Nitrotoluene is liquid at the ordinary temperature, its melting-point being −3·4°; *p*-nitrotoluene

is solid, and melts at 51·4°. These isomerides are separated by a combination of repeated solidification by cooling and of fractional distillation. Fig. 70 represents the fusion-curve ("Inorganic Chemistry," 239) of mixtures of *o*-nitrotoluene and *p*-nitrotoluene. As the nitration-product contains about 40 per cent of the *para*-isomeride, its freezing-point lies on the *para*-section of the curve, and cooling causes crystallization of *p*-nitrotoluene. This substance can be separated from the liquid residue by filtration, or on the manufacturing scale by centrifuging. The first product of the fractional distillation of the oil is *o*-nitrotoluene, boiling at 218°; subsequently *p*-nitrotoluene, boiling at 234°, distils. Several repetitions of the fractional distillation, with

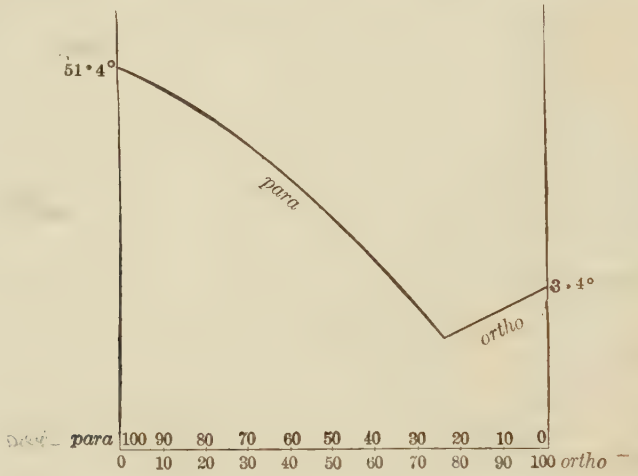


FIG. 70.—FUSION-CURVE OF MIXTURES OF *o*-NITROTOLUENE AND *p*-NITROTOLUENE.

intermediate solidification by cooling, finally yield an initial fraction so rich in the *ortho*-compound that its composition pertains to the *ortho*-section of the curve. Cooling of this fraction induces crystallization of *o*-nitrotoluene.

III. MONOSULPHONIC ACIDS.

291. The formation of these compounds by the action of concentrated sulphuric acid on aromatic compounds is described in **282**, 2. In this reaction a considerable proportion of the sulphuric acid does not combine, for sulphonation ceases when the strength of the acid has fallen to 64 per cent. The method employed in the separation of the sulphonic acid from the excess of sulphuric acid is similar to that

adopted for the separation of ethylsulphuric acid (54), the barium salts of the aromatic sulphonic acids being readily soluble in water. Another method of isolation involves the addition of a concentrated solution of common salt to the mixture of sulphuric acid and sulphonic acid, the solid sodium sulphonate being precipitated.

When the sulphuric acid is heated to 170°, and benzene-vapour is passed into it, the whole of the acid is converted into benzenesulphonic acid. Under these conditions the water formed by the sulphonation distils, the sulphuric acid being maintained throughout at a concentration suitable for sulphonation.

The sulphonic acids are colourless crystalline substances, generally hygroscopic, and freely soluble in water. They can be reconverted into the aromatic hydrocarbons by hydrochloric acid or superheated steam at a high temperature (284, 5), a reaction discovered by ARMSTRONG.

Most of the sulphonates crystallize well, and are employed in the purification of the sulphonic acids. Phosphorus pentachloride converts these acids into chlorides:

$$C_6H_5 \cdot SO_2 \cdot OH \rightarrow C_6H_5 \cdot SO_2 \cdot Cl.$$

The *sulphonyl chlorides* can be obtained also directly by the interaction of chlorosulphonic acid and aromatic hydrocarbons:

$$C_6H_6 + HO \cdot SO_2 \cdot Cl = C_6H_5 \cdot SO_2 \cdot Cl + H_2O.$$

They are very stable towards cold water, being only slowly reconverted into sulphonic acids. *Benzenesulphonyl chloride* melts at 14·5°. Like the other sulphonyl chlorides, it has a very disagreeable odour.

The *sulphonamides* are formed by the action of excess of concentrated ammonia on the chlorides:

$$C_6H_5 \cdot SO_2Cl \rightarrow C_6H_5 \cdot SO_2 \cdot NH_2.$$

Initially the sulphonyl chloride dissolves, the sulphonamide being precipitated by addition of acid.

They are well-crystallized compounds, and the determination of their melting-points often is employed for the identification of aromatic hydrocarbons. The strongly negative character of the benzenesulphonyl-group renders the hydrogen atoms of the amino-group replaceable by metals, the sulphonamides being soluble in alkalis and in ammonia.

Prolonged reduction of sulphonic acids yields *thiophenols* of the

type $C_6H_5 \cdot SH$, substances reconvertible into sulphonic acids by oxidation.

The sulpho-group can be replaced by the hydroxyl-group and the cyano-group (**292** and **311**).

IV. MONOHYDRIC PHENOLS.

292. The *phenols* are compounds derived from the aromatic hydrocarbons by replacement of one or more of the hydrogen atoms of the nucleus by hydroxyl.

Phenol, $C_6H_5 \cdot OH$, and some of its homologues such as *cresol* and others are present in coal-tar. During its fractional distillation they are accumulated in the carbolic oil and the creosote-oil (**283**). They are isolated by agitating these fractions with caustic alkali, the phenols going into solution, and the hydrocarbons remaining undissolved. They are liberated from the solution by sulphuric acid, and are separated by fractional distillation. By far the larger proportion of the phenol of commerce is obtained from this source.

Phenol and its homologues can be obtained also by other methods:

1. By fusion of the salt of a sulphonic acid with an alkali-metal hydroxide:

$$C_6H_5 \cdot SO_3K + 2KOH = C_6H_5 \cdot OK + K_2SO_3 + H_2O.$$

2. By the action of nitrous acid on aromatic amines, a method analogous to the preparation from amines of alcohols of the aliphatic series (**65**). An aliphatic amine reacts with nitrous acid to produce the alcohol directly, but in this process the very important intermediate diazonium compounds (**305**) can be isolated.

3. By the combination of oxygen and benzene in presence of aluminium chloride, phenol is formed.

293. In some respects the phenols are comparable with the tertiary alcohols, the hydroxyl of each type being attached to a carbon atom in direct union with three others, although in the phenols one of these bonds is of a special kind. Like the tertiary alcohols, they cannot be oxidized to aldehydes, ketones, or acids containing the same number of carbon atoms. The phenols exhibit many of the characteristics of the aliphatic alcohols. This resemblance is exemplified by the formation of ethers by the interaction of alkyl halides and their alkali-metal salts; and by the production with acetyl chloride of esters such as acetates. Phosphorus pentachloride replaces their hydroxyl by chlorine, although not so readily as in the aliphatic series. Besides these properties, the phenols possess special characteristics due to their having a much

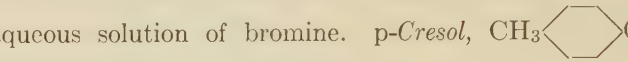
stronger acidic character than the alcohols. The description of the separation of phenols from carbolic oil (292) mentions their solubility in caustic alkalis, *phenoxides* such as sodium phenoxide, $C_6H_5 \cdot ONa$, being formed. The alcohols of the aliphatic series do not possess this property in the same degree. If insoluble in water, they do not dissolve in caustic alkalis, and are converted into metallic alkoxides only by the action of the alkali-metals. This increase in acidic character can be occasioned only by the presence of the phenyl-group, *and indicates the phenyl-group to have a more negative character than an alkyl-group.* The phenols behave as weak acids only, their aqueous solutions being bad conductors of electricity, and the phenoxides being decomposed by carbon dioxide.

Obviously the properties of the hydroxyl-group are modified considerably by union with the phenyl-group. Inversely, the influence of the hydroxyl-group on the benzene-nucleus is equally marked, for it facilitates considerably substitution of the remaining hydrogen atoms. At the ordinary temperature benzene is attacked by bromine slowly, but the addition of bromine-water to a cold aqueous solution of phenol precipitates 2:4:6-*tribromophenol* instantaneously, a reaction employed in its quantitative estimation. The conversion of benzene into nitrobenzene requires concentrated nitric acid, but with the dilute acid phenol yields nitrophenol. Phenols also are oxidized much more readily than the aromatic hydrocarbons. Heating them with zinc ammonium chloride replaces the hydroxyl-group by the amino-group.

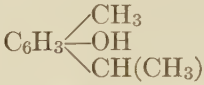
Distillation with zinc-dust reduces the phenols to the corresponding hydrocarbons. Phenols can be detected by the formation of a violet coloration following addition of ferric chloride to their aqueous solutions, probably due to the production of a ferric salt of the phenol.

294. *Phenol* or *carbolic acid* is a colourless substance crystallizing in long needles. It melts at 39·6°, boils without decomposition at 181°, and has a characteristic odour. Its powerful antiseptic properties caused its introduction into surgery by Lister, but to a great extent its place has been taken by mercuric chloride. Phenol is soluble in water, one part dissolving in fifteen parts at 16°, and it also can dissolve water. On account of the small molecular weight of water, and the high molecular depression of phenol (75), a small percentage of water renders phenol liquid at the ordinary temperature (12). The equation $AM = 75$, M being the molecular weight of water (18), indicates the lowering A of the freezing-point occasioned by the presence of one per cent. of water to be about 4·2°.

The hydroxytoluenes, $CH_3 \cdot C_6H_4 \cdot OH$, are termed *cresols*. They are present in coal-tar, but usually are prepared from the corresponding

amino-compounds or sulphonic acids. Oxidation decomposes them completely, but replacement of the hydrogen of the hydroxyl-group by alkyl or acetyl enables them to be oxidized like toluene to the corresponding acids. The cresols resemble phenol in their behaviour towards an aqueous solution of bromine. p-*Cresol*,  , is a decomposition-product of albumin.

Thymol also is employed as an antiseptic. It is hydroxycymene,



The fusion of phenols with formaldehyde yields characteristic, resin-like products of yellow colour. They are transformed by heat into a beautiful substance with the transparency of amber. These "Phenolic resins" are named "Bakelite" after their discoverer BAEKELAND, and are employed in the production of a great variety of articles.

Ethers.

295. A distinction is drawn between the aromatic-aliphatic ethers such as *anisole*, $C_6H_5 \cdot O \cdot CH_3$, and the true aromatic ethers like *diphenyl ether*, $C_6H_5 \cdot O \cdot C_6H_5$. Compounds of the first class are formed by the interaction of alkyl halides or dimethyl sulphate and phenoxides (**293**):

$$C_6H_5 \cdot O \cdot \boxed{Na+I}\, C_2H_5 = C_6H_5 \cdot O \cdot C_2H_5 + NaI.$$

The true aromatic ethers cannot be prepared by this method, the halogen atom attached to the nucleus being exchanged only with difficulty (**289**). *Diphenyl ether* is obtained by passing vaporized phenol over heated thorium oxide:

$$C_6H_5 \cdot \boxed{OH+H}\, O \cdot C_6H_5 = C_6H_5 \cdot O \cdot C_6H_5 + H_2O.$$

The mixed aromatic-aliphatic ethers are stable compounds, and in behaviour closely resemble the true aliphatic ethers. Many of their reactions are similar to those of the aromatic hydrocarbons. Heating them to a high temperature with a hydrogen halide yields a phenol and an alkyl halide:

$$\underset{\text{Anisole}}{C_6H_5 \cdot O \cdot CH_3} + HI = C_6H_5 \cdot OH + CH_3 \cdot I.$$

The true aromatic ethers such as diphenyl ether are not decomposed by hydrogen iodide, even at 250°.

Anisole, $C_6H_5 \cdot O \cdot CH_3$, is a liquid, and boils at 155°. *Phenetole*, $C_6H_5 \cdot O \cdot C_2H_5$, also is a liquid, and boils at 172°. Each of these compounds has a lower boiling-point than phenol (**294**), and each has a characteristic odour.

V. MONOAMINO-COMPOUNDS.

296. The amino-compounds of the aromatic series with the amino-group attached to the ring are obtained almost exclusively by reduction of the corresponding nitro-compounds. This process is effected by various means.

Amines can be obtained from phenols by heating them at 300° with ammonium zinc chloride.

The aromatic amines are colourless liquids, or solids, and have a characteristic odour. They are only slightly soluble in water. Their densities approximate to 1, and their boiling-points lie above 180°. With water the aliphatic amines form stronger bases than ammonia; but the aqueous solutions of the aromatic amines possess only weakly basic properties, for they do not turn red litmus blue, and scarcely conduct the electric current. The aromatic amines do yield salts, although these derivatives in solution have an acidic reaction on account of partial hydrolysis. The negative character of the phenyl-group, mentioned already in connexion with phenol (**293**), modifies the nature of the amino-group considerably, an influence exhibited in an even more marked degree by the difference in the behaviour of diphenylamine and of triphenylamine. With strong acids the secondary amine can yield salts, although they are hydrolyzed completely by the addition of a considerable proportion of water; but the tertiary amine does not unite with acids.

Diphenylamine picrate furnishes another example of the hydrolysis of salts of the base. The picrate is brown, picric acid yellow, and diphenylamine colourless. The salt and the free base are only slightly soluble in water, and picric acid is moderately soluble. The hydrolytic equilibrium corresponds with the expression

$$\text{Salt} + \text{Water} \rightleftarrows \text{Acid} + \text{Base},$$

and since the mass of the water can be regarded as constant owing to the large amount present, application of the law of mass action in this instance gives the expression

$$\text{Concentration}_{acid} = \text{Constant}.$$

The concentrations of the salt and of the diphenylamine also are constant, owing to the solution being saturated continually by contact with the solids.

At 40·6° the constant concentration of the acid has been determined to be thirteen grammes per litre. When a solution of picric acid of this concentration is poured on solid diphenylamine, the salt does not form,

owing to complete hydrolysis. Increase in the concentration of the picric acid imparts a brown colour to the diphenylamine, this phenomenon arising from the formation of the salt, and persisting until the concentration has fallen to thirteen grammes per litre.

Substitution of the amino-group for hydrogen produces the same effect on the benzene-nucleus as exchange of the hydroxyl-group for hydrogen, facilitating greatly replacement of the other hydrogen atoms of the nucleus. As a result, at the ordinary temperature aniline is converted readily by bromine-water into 2:4:6-tribromoaniline. The amines also are oxidized much more easily than the hydrocarbons.

By means of an alkyl halide the hydrogen atoms in the amino-group of the primary aromatic amines, like those in the amino-group of the primary aliphatic amines, can be replaced by an alkyl-group (**63**):

$$C_6H_5\cdot NH_2+CH_3I=C_6H_5\cdot NH(CH_3),HI.$$

Secondary and tertiary bases, and also quaternary ammonium bases such as $C_6H_5\cdot N(CH_3)_3\cdot OH$, are known. The last are as strongly basic as the corresponding true aliphatic compounds.

The *anilides* are derivatives of aniline, $C_6H_5\cdot NH_2$, and its homologues. They are acid amides with one amino-hydrogen atom replaced by a phenyl-group. *Acetoanilide*, $C_6H_5\cdot NH\cdot COCH_3$, employed as a febrifuge under the name " antifebrine," is a type of these compounds. The anilides are produced by boiling aniline with the corresponding acid, acetoanilide being obtained by heating aniline with glacial acetic acid:

$$C_6H_5\cdot NH\boxed{H+HO}OC\cdot CH_3=C_6H_5\cdot NH\cdot COCH_3+H_2O.$$

Like the acid amides of the aliphatic series (**96**), the anilides are decomposed readily into their parent substances by boiling with a dilute solution of an alkali-metal hydroxide or of a mineral acid.

Menschutkin found the velocity of formation of acetoanilide to be much less for an excess of aniline than for an excess of glacial acetic acid, although on theoretical grounds it should be the same for both. At each moment it should be proportional to the product of the concentrations of the glacial acetic acid (c) and of the aniline (c'), being expressed therefore by

$$s=k\cdot cc',$$

k being constant.

The discrepancy between theory and experiment admits of various explanations, such as the difference between the reaction-media. The important influence of the medium is mentioned in **64**.

Aldehydes react with aromatic amines with elimination of water:

$$\underset{\text{Formaldehyde}}{H_2C\boxed{O+\begin{matrix}H\\H\end{matrix}}}\begin{matrix}HNC_6H_5\\HNC_6H_5\end{matrix}=H_2C<\underset{\text{Methylenediphenyldiamine}}{\begin{matrix}NHC_6H_5\\NHC_6H_5\end{matrix}}+H_2O.$$

The combination of aromatic aldehydes and aromatic amines is exemplified by the equation

$$\underset{\text{Benzaldehyde}}{C_6H_5\cdot CH\boxed{O+H_2}}N\cdot C_6H_5=\underset{\text{Benzalaniline}}{C_6H_5\cdot CH:NH\cdot C_6H_5}+H_2O.$$

Primary aromatic amines give the carbylamine-reaction, and with nitrous acid they yield diazonium compounds (305).

Aniline.

297. Aniline was obtained first by the dry distillation of indigo (Portugese, *anil*; from Sanskrit, *nīla*, dark-blue, and *nīlā*, the indigo-plant), and to this fact it owes its name. It is manufactured by the action of hydrochloric acid and iron-filings on nitrobenzene contained in a cast-iron cylinder fitted with a stirrer:

$$C_6H_5NO_2+3Fe+6HCl=C_6H_5NH_2+2H_2O+3FeCl_2.$$

In this process only about one-fortieth of the hydrochloric acid required by the equation is needed for the reduction. This remarkable phenomenon probably originates in the capacity of iron-filings and water to effect the reduction in presence of ferrous chloride. Lime is added after completion of the reduction, and the aniline is distilled with steam.

Aniline is obtained also by the electro-reduction of nitrobenzene (303).

Aniline is a colourless liquid, but unless perfectly pure it turns brown in the air, the colour-change probably being due to the presence of traces of sulphur compounds. It is only slightly soluble in water. It boils at 183°, and at 16° has the density 1·024. With aniline formaldehyde yields a remarkable condensation-product, *anhydroformaldehydeaniline*, $(C_6H_5N{=}CH_2)_3$. This substance melts at 40°, and dissolves with difficulty. It is employed in the identification of both formaldehyde (108) and aniline.

An aqueous solution of free aniline gives a deep-violet coloration with bleaching-powder solution, the primary product in the reaction probably being *phenylchloroamine*, $C_6H_5\cdot NHCl$, the reaction being analogous to the formation of chloroamine, NH_2Cl, from ammonia.

The phenylchloroamine condenses with the aniline to form coloured substances. An aniline salt in acid solution is coloured dark-green to black by potassium dichromate. These two reactions, and that with wood (228), serve as tests for aniline. The bleaching-powder reaction is particularly delicate. The oxidation of aniline is discussed in 338.

Homologues of Aniline.

Ortho-*toluidine* and para-*toluidine*, $CH_3 \cdot C_6H_4 \cdot NH_2$, are formed by the reduction of the corresponding nitro-compounds. The *ortho*-compound is a liquid boiling at 199·4°; the *para*-compound is a solid melting at 45°. The different solubilities of their oxalic-acid salts afford a means of separating them.

The monoamino-derivatives of the xylenes are termed *xylidines*. Six isomerides are possible, their existence being due to differences in the relative positions of the methyl-groups and the amino-group in the ring. Some of the toluidines and the xylidines are employed in making coal-tar colours, and therefore are manufactured in large quantities.

Secondary Amines.

298. *Diphenylamine*, $C_6H_5 \cdot NH \cdot C_6H_5$, melts at 54°, and boils at 310°. It is a type of the true secondary aromatic amines. They are formed by heating the hydrochlorides of the primary amines with the free amines:

$$C_6H_5\boxed{NH_2,HCl + H}HN \cdot C_6H_5 = NH_4Cl + HN(C_6H_5)_2.$$

Diphenylamine can be obtained also by the action of bromobenzene on potassium anilide, $C_6H_5 \cdot NHK$. It has an agreeable floral odour.

Diphenylamine is a very sensitive reagent for the detection of nitric acid, that substance producing a deep-blue colour with its solution in concentrated sulphuric acid. The reaction can be applied to the detection of nitric acid only in the absence of other oxidizers such as bromine-water and permanganate, for diphenylamine also gives a blue coloration with many of these reagents. The blue coloration arises from the formation of the quinonoid salt of *NN'*-diphenylbenzidine (**301**),

The method of formation of the mixed aromatic-aliphatic amines such as *methylaniline*, $C_6H_5 \cdot NH \cdot CH_3$, is indicated in **296**. The action

of the alkyl iodide on aniline effects the substitution of more than one hydrogen atom of the amino-group by an alkyl-group, a mixture of the unchanged primary amine with the secondary and tertiary amines being formed. The pure secondary amine is obtained by initial replacement of one hydrogen atom of the amino-group by an acid-radical such as acetyl, and subsequent interaction of the acetyl-derivative and an alkyl iodide.

In preparing such a compound as methylaniline, the first step is to convert aniline into acetoanilide, $C_6H_5 \cdot NH \cdot COCH_3$, by boiling it with glacial acetic acid. The hydrogen atom attached to nitrogen in this compound can be replaced by sodium, yielding $C_6H_5 \cdot NNa \cdot COCH_3$, a substance transformed by methyl iodide into *methylacetoanilide*, $C_6H_5 \cdot N(CH_3) \cdot COCH_3$. Saponification with alkalis converts this compound into monomethylaniline.

The secondary aromatic amines resemble those of the aliphatic series in their ready conversion by nitrous acid into nitrosoamines such as *nitrosomethylaniline*, $C_6H_5 \cdot N{<}\begin{matrix}NO\\CH_3\end{matrix}$. LIEBERMANN'S *reaction* for nitroso-compounds is described in "Laboratory Manual," XXVII, 11.

Careful oxidation of the nitrosoamines transforms them into *nitroamines*, $C_6H_5 \cdot N{<}\begin{matrix}NO_2\\R\end{matrix}$. Compounds of this type are produced also by the direct action of fuming nitric acid on secondary amines such as methylaniline or ethylaniline, three nitro-groups entering the nucleus simultaneously. FRANCHIMONT has prepared a large number of nitroamines belonging to the aliphatic series (270).

Tertiary Amines.

299. *Triphenylamine*, $(C_6H_5)_3N$, is a type of the true aromatic tertiary amines, only a few of them being known. It is obtained by the action of sodium and bromobenzene on diphenylamine, and is a solid melting at 127°. It does not possess a basic character.

Although perchloric acid, $HClO_4$, can unite with triphenylamine, the special aptitude of this acid for combination with many substances, both nitrogenous and non-nitrogenous, must not be overlooked.

Dimethylaniline, $C_6H_5 \cdot N{<}\begin{matrix}CH_3\\CH_3\end{matrix}$, is the most important member of the series of mixed aromatic-aliphatic tertiary amines. They can be obtained by the action of alkyl halides on aniline, but they are manu-

factured by heating aniline hydrochloride with the alcohol, a method enabling the alkyl halides to react in the nascent state. Methyl alcohol and hydrogen chloride yield methyl chloride, and this compound attacks the aniline.

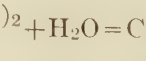
On heating the hydrochloride of an alkyl-aniline at 180°, in a current of gaseous hydrogen chloride, the alkyl-groups are eliminated, with formation of aniline and an alkyl chloride, the last-named compound uniting with unchanged alkyl-aniline to form a trialkylphenylammonium chloride. When this substance is heated, the alkyl-groups become transposed from the nitrogen to the nucleus. Free methylaniline or dimethylaniline are unaffected by heat.

The formation of the hydrochloride of *p*-toluidine by the interaction of methyl alcohol and aniline hydrochloride at a high temperature is analogous. By this process it is possible to obtain even *pentamethylaminobenzene*, $C_6(CH_3)_5 \cdot NH_2$.

The *para*-hydrogen atoms of dimethylaniline and of other dialkylanilines are replaceable by various groups, dimethylaniline reacting readily with nitrous acid to form *nitrosodimethylaniline*,

This operation is effected by the addition of potassium nitrite to the solution of the tertiary base in hydrochloric acid. This nitroso-compound crystallizes in well-defined leaves of a fine green colour. It melts at 85°, and yields a hydrochloride crystallizing in yellow needles. Oxidation with potassium permanganate converts the nitroso-group into a nitro-group, and forms p-*nitrodimethylaniline*,

Boiling with sodium hydroxide removes the amino-group of nitrosodimethylaniline, yielding dimethylamine and nitrosophenol:



Nitrosophenol

This reaction is employed in the preparation of pure dimethylamine (66).

The *para*-hydrogen atom of dimethylaniline can react with substances other than nitrous acid, aldehydes readily yielding a condensation-product:

$$C_6H_5\cdot CH\boxed{O+\begin{matrix}H\\H\end{matrix}}\begin{matrix}C_6H_4N(CH_3)_2\\C_6H_4N(CH_3)_2\end{matrix}=C_6H_5\cdot\overset{1}{C}H[C_6H_4\overset{4}{N}(CH_3)_2]_2.$$

The constitution of this compound is inferred from its relation to *triphenylmethane*, $CH(C_6H_5)_3$ (**373**). Dimethylaniline and carbonyl chloride yield a *p*-derivative of benzophenone, $C_6H_5\cdot CO\cdot C_6H_5$, termed MICHLER'S ketone:

$$\begin{matrix}\diagup\\CO\\\diagdown\end{matrix}\boxed{\begin{matrix}Cl+H\\\\Cl+H\end{matrix}}\begin{matrix}C_6H_4\cdot N(CH_3)_2\\\\C_6H_4\cdot N(CH_3)_2\end{matrix}=\begin{matrix}\overset{1}{\diagup}C_6H_4\cdot\overset{4}{N}(CH_3)_2\\CO\\\diagdown C_6H_4\cdot\overset{4}{N}(CH_3)_2\end{matrix}+2HCl.$$

Heating with fuming nitric acid converts dimethylaniline into *trinitrophenylnitroamine*,

$$(NO_2)_3C_6H_2\cdot N\begin{matrix}\diagup CH_3\\\diagdown NO_2\end{matrix},$$

the reaction being accompanied by a copious evolution of gas. This compound is employed as an explosive. In its formation one of the methyl-groups is removed by oxidation and replaced by the nitro-group, three additional nitro-groups being introduced simultaneously into the nucleus. The reaction affords a general method for the formation of nitroamines.

Quaternary Bases.

Quaternary bases are formed by the addition of alkyl halides to the tertiary aromatic-aliphatic amines, and the interaction of the salts formed and moist silver oxide. These substances are strong bases. Heating transforms them into an alcohol and a tertiary amine, a difference from the aliphatic ammonium bases (**66**).

VI. INTERMEDIATE PRODUCTS IN THE REDUCTION OF AROMATIC NITRO-COMPOUNDS.

300. Reduction of the nitro-compounds of the aliphatic series yields amines directly, and from them the alkyl-groups can be removed by oxidation. An example is the conversion of ethylamine into acetic acid and ammonia. In contrast, in the aromatic series intermediate

products can be obtained in the reduction of nitro-compounds, and sometimes also in the oxidation of amines. Only the compounds derived from nitrobenzene and aniline will be described here, although numerous substitution-products of the same type are known.

In acid solution the nitro-compounds are reduced directly to the corresponding amino-derivatives, but in alkaline solution they yield substances containing two benzene-residues. Nitrobenzene gives in succession *azoxybenzene*, *azobenzene*, *hydrazobenzene*, and aniline:

1. Nitro-compound, $C_6H_5 \cdot NO_2$ $O_2N \cdot C_6H_5$;
2. *Azoxy-compound*, $C_6H_5 \cdot N(\rightarrow O) - N \cdot C_6H_5$;
3. *Azo-compound*, $C_6H_5 \cdot N{=}N \cdot C_6H_5$;
4. *Hydrazo-compound*, $C_6H_5 \cdot NH{-}NH \cdot C_6H_5$;
5. Amino-compound, $C_6H_5 \cdot NH_2$ $H_2N \cdot C_6H_5$.

Azoxybenzene is obtained by boiling nitrobenzene with alcoholic potassium hydroxide, and is produced also in the oxidation of aniline with potassium permanganate in alcoholic solution. It forms light-yellow crystals melting at 36°. Warming with concentrated sulphuric acid transforms it into p-*hydroxyazobenzene:*

$$C_6H_5 \cdot N(\rightarrow O) - N \cdot C_6H_5 \rightarrow \underset{\text{Hydroxyazobenzene}}{C_6H_5 \cdot N{=}N \cdot C_6H_4 \cdot OH}.$$

It is attacked readily by various reducers. Under the influence of direct sunlight concentrated sulphuric acid converts azoxybenzene into o-*hydroxyazobenzene.*

p-*Azoxyphenetole*, $C_2H_5O \cdot C_6H_4 \cdot N(\rightarrow O) - N \cdot C_6H_4 \cdot OC_2H_5$, is distinguished by its power of forming a *crystalline liquid*, a property characteristic of a considerable number of other substances. When heated, it melts at 134° to a turbid liquid, suddenly becoming clear at 165°. The crystalline structure of the turbid liquid cannot be observed with the microscope, but it is indicated by the double refraction exhibited by the liquid, and by the formation of the figures characteristic of double-refracting crystals between crossed Nicol prisms in converging light.

Turbidity is not an essential characteristic of crystalline liquids, as Vorländer has discovered perfectly clear liquids displaying phenomena like those of double-refracting crystals. The power of forming crystalline liquids is a characteristic chiefly of compounds with normal carbon chains, and of the *para*-compounds among the benzene derivatives.

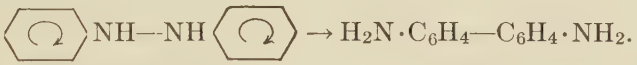
301. *Azobenzene*, $C_6H_5 \cdot N{:}N \cdot C_6H_5$ is formed by the reduction of nitrobenzene with a solution of stannous chloride in excess of potassium

hydroxide, and also by distilling azoxybenzene with iron-filings. It is produced along with azoxybenzene by the oxidation of aniline with potassium permanganate.

Azobenzene forms well-defined orange-red crystals melting at 68°, and boiling without decomposition at 295°. It is a very stable compound, and is insoluble in water. Its constitution follows from its yielding aniline by reduction.

Hydrazobenzene, $C_6H_5 \cdot NH—NH \cdot C_6H_5$, is formed by the action of zinc-dust and alcoholic potassium hydroxide on azobenzene or nitrobenzene. It is a colourless crystalline substance melting at 126°. Strong reducers convert it into aniline; but it is oxidized readily to azobenzene, the transformation being effected slowly by atmospheric oxygen. It is oxidized to the azo-compound by ferric chloride also.

The most characteristic reaction of hydrazobenzene is its conversion into *benzidine*, the benzene-nuclei becoming turned end for end. This "benzidine-transformation" is effected by the action of strong acids:

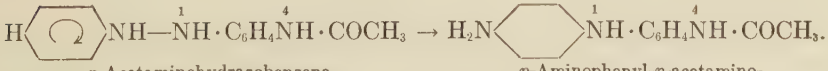


Hydrazobenzene — Benzidine

The formation of a diaminodiphenyl is proved by the conversion of benzidine into diphenyl, $C_6H_5 \cdot C_6H_5$. The amino-groups occupy the *para*-positions:

Reduction of azobenzene in acid solution forms benzidine directly. It is characterized by the sparing solubility in cold water of its sulphate.

The amino-groups in benzidine are proved in various ways to occupy the *para*-position, one being the impracticability of converting into benzidine a hydrazobenzene with its *p*-hydrogen atoms substituted. In certain instances hydrazo-compounds can undergo a remarkable intramolecular change, known as the "semidine-transformation," derivatives of diphenylamine being formed by the turning of only one of the benzene-nuclei:



p-Acetaminohydrazobenzene — *p*-Aminophenyl-*p*-acetamino-phenylamine

Electro-reduction of Nitro-compounds.

302. In electrolytic reductions or oxidations the course of the chemical reactions at the electrodes are controlled by various factors.

Electrolytic reduction will be considered first. In the electrolysis of a solution of an acid with a hydrogen-ion concentration equal to 1-normal, the hydrogen ions are discharged when there is a certain difference of potential between the electrolyte and the cathode; and with a platinum cathode this difference of potential is practically identical with the equilibrium-potential of a normal hydrogen electrode. This potential serves as the zero for measurements of potential, and usually is given the value $E = 0$. On the other hand, when a cathode of lead or mercury is employed in the electrolysis of a solution of the type mentioned the hydrogen ions undergo discharge only when the difference of potential between the electrolyte and the cathode has a value much more negative than zero; and under these conditions its value can be even more negative than -1 volt. The phenomenon is termed *overvoltage*, and with the cathodes cited a high degree of overvoltage can be attained.

Experiment has demonstrated many substances reducible with difficulty, and not reducible at a platinum cathode, to be capable of undergoing ready reduction at a cathode characterized by overvoltage. By choosing an appropriate material for the cathode, it is, therefore, possible by means of the electrical process to effect the reduction of some substances not reducible by any other method.

Another factor of importance in electrolytic processes is the *current density*, or the strength of the current in ampères divided by the surface-area of the electrode in square decimètres. The number of ions discharged in the unit of time and per unit of electrode surface is proportional to the current density.

In electrolytic processes dependent on the mutual interaction of the discharged ions a high current density is necessary, and is attained by making the surface-area of the electrode where the reaction occurs small. By this means a high concentration of the discharged ions is maintained in the immediate neighbourhood of the electrode. This condition is exemplified by the formation of ethane in the electrolysis of acetic acid by KOLBE'S method, the anions reacting at the anode in accordance with the scheme.

$$2CH_3COO' \rightarrow 2CO_2 + C_2H_6.$$

In electrolytic reductions requiring the hydrogen ions discharged at the cathode to react with the dissolved substance, it is important for the surface of contact between the liquid and the cathode to be large, and for such an operation a large cathode surface and a small current density are employed. When a high overvoltage is required for an

electrolytic reduction, it is desirable to have a large current density, and a cathode of small surface-area is chosen.

The reduction of nitro-compounds ultimately yields amines, but a number of intermediate reduction-products can be isolated. For this reason the electro-reduction of nitrobenzene and its derivatives is of both theoretical and practical importance. It is possible to give a complete and satisfactory explanation of the mechanism of this process.

303. A distinction must be drawn between primary or electrolytic reduction-products and secondary or chemical reduction-products. The primary process is indicated by the scheme

$$\underset{\text{Nitrobenzene}}{C_6H_5\cdot NO_2} \rightarrow \underset{\text{Nitrosobenzene}}{C_6H_5NO} \rightarrow \underset{\text{Phenylhydroxylamine}}{C_6H_5\cdot NHOH} \rightarrow \underset{\text{Aniline}}{C_6H_5\cdot NH_2}.$$

The presence of nitrosobenzene can be detected by the addition of hydroxylamine to the liquid, that substance reacting with loss of one molecule of water and formation of benzenediazonium hydroxide, $C_6H_5\cdot N_2\cdot OH$. Addition of α-naphthol produces an azo-dye (340). The formation of phenylhydroxylamine can be detected by adding benzaldehyde, *benzylidenephenylhydroxylamine* being generated:

$$C_6H_5\cdot NHOH + \underset{\text{Benzaldehyde}}{OCH\cdot C_6H_5} = H_2O + \begin{array}{c} C_6H_5\cdot N\text{———}CH\cdot C_6H_5 \\ \diagdown\ \diagup \\ O \end{array}.$$

The rapid reduction of nitrobenzene dissolved in moderately concentrated sulphuric acid, with the addition of alcohol to increase the solubility, follows the primary process described, about 90 per cent. of the theoretical yield of aniline being obtained. In a strongly acid solution the course of the reaction is different, the *phenylhydroxylamine* being converted very quickly into p-*aminophenol:*

$$C_6H_5\cdot NHOH \rightarrow HO\cdot C_6H_4\cdot NH_2.$$

This substance is not reduced further. Since in presence of more dilute acid phenylhydroxylamine undergoes the same transformation, though much more slowly, obviously the theoretical yield of aniline cannot be obtained, even with a dilute solvent and a great reduction-velocity.

304. In alcoholic-alkaline solution the electro-reduction of nitrobenzene is accompanied by two secondary processes:

1. Nitrosobenzene reacts with phenylhydroxylamine, yielding azoxybenzene:

$$C_6H_5\cdot NHOH + C_6H_5\cdot NO = \begin{array}{c} C_6H_5\cdot N\text{———}N\cdot C_6H_5 \\ \diagdown\ \diagup \\ O \end{array} + H_2O.$$

In presence of alkali this reaction proceeds much more quickly than the further reduction of phenylhydroxylamine, aniline being formed in small proportion only. The main part of the yield consists of the higher reduction-products of azoxybenzene, the chief being hydrazobenzene.

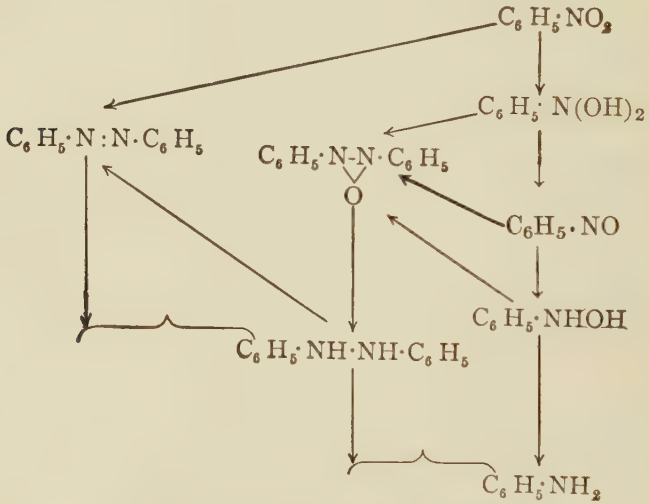
2. Hydrazobenzene is attacked by the unreduced nitrobenzene with formation of azobenzene and azoxybenzene:

$$3C_6H_5\cdot NH\cdot NH\cdot C_6H_5+2C_6H_5\cdot NO_2=3C_6H_5\cdot N:N\cdot C_6H_5+$$
$$+\ C_6H_5\cdot N\langle O\rangle N\cdot C_6H_5+3H_2O.$$

Hydrazobenzene in alkaline solution being oxidized quickly to azobenzene by atmospheric oxygen, the yield of that derivative is very good.

A much higher contact-difference of potential at the cathode is required to reduce hydrazobenzene to aniline. In the formation of nitrosobenzene and phenylhydroxylamine a difference of about 0·93 volt is necessary, but with a difference of 1·47 volt only traces of aniline are formed from hydrazobenzene.

Haber has combined these primary and secondary reactions in the subjoined scheme, the vertical arrows indicating primary reactions and the oblique arrows secondary reactions.



Haber's Electro-reduction Scheme.

Bamberger noted the reduction of nitrobenzene by purely chemical methods to yield the same intermediate products, nitrosobenzene being formed by its interaction with zinc-dust and water. In accord with this view is the fact that the velocity of reduction of nitrobenzene by stannous chloride in presence of a great excess of hydrogen-chloride solution indicates the reaction to be bimolecular, and therefore to be represented by the equation

$$R\cdot NO_2+SnCl_2+nHCl=R\cdot NO+SnCl_4+H_2O+(n-2)HCl.$$

This reaction has a measurable velocity. The further reduction of the nitroso-compound to the amino-compound should be very rapid, and experi-

mental confirmation of this theoretical view is afforded by the instantaneous reduction of nitrosodimethylaniline through contact with stannous chloride.

VII. DIAZO-COMPOUNDS.

305. The diazo-compounds of the aromatic series were discovered by GRIESS in 1860. They are not merely of theoretical importance, but play an important part in the manufacture of dyestuffs. In the aliphatic series only amino-compounds of a special kind yield diazo-compounds (245), but their formation is a general reaction of the primary aromatic amines. *The property of undergoing diazotization is characteristic of aromatic amines.*

All diazo-compounds contain the group —N_2—. HANTZSCH classified them in two divisions:

I. Substances with the structural formula $\begin{matrix} Ar\cdot N\cdot X \\ \| \\ N \end{matrix}$, Ar representing phenyl, C_6H_5, and its homologues and derivatives. They are termed *diazonium salts*, and are analogous to the ammonium salts.

II. Substances with the structural formula $Ar\cdot N{=}N\cdot X$. These derivatives are named *diazo-compounds*, and resemble the azo-compounds. They are known in two stereoisomeric modifications:

1. syn*Diazo-compounds* with the stereochemical formula $\begin{matrix} Ar\cdot N \\ \| \\ X\cdot N \end{matrix}$. They are unstable, and only a few of them have been isolated.

2. anti*Diazo-compounds* with the stereochemical formula $\begin{matrix} Ar\cdot N \\ \| \\ N\cdot X \end{matrix}$. These substances are stable.

Intrinsically the diazonium compounds are of slight importance, but their numerous transformations to form a great number of derivatives render them much more important than the diazo-compounds, and give them great significance in the chemistry of the aromatic compounds.

Diazonium compounds are produced by the action of nitrous acid on the salts of aromatic amines:

$$\underset{\text{Aniline nitrate}}{C_6H_5\cdot NH_2,HNO_3} + HNO_2 = 2H_2O + \underset{\text{Benzenediazonium nitrate}}{C_6H_5\cdot N_2\cdot NO_3}.$$

This reaction is effected by adding a solution of sodium nitrite to one containing an equimolecular proportion of the amine-salt and an equivalent quantity of a free mineral acid. The reaction-mixture is cooled by the addition of ice, the diazonium compounds decomposing very readily. A solution of the benzenediazonium salt is obtained by the process.

The preparation in the solid state of a salt such as *benzenediazonium nitrate*, $C_6H_5 \cdot N_2 \cdot NO_3$, involves passing nitrogen trioxide generated from nitric acid and arsenious oxide into a solution of aniline in dilute nitric acid. The addition of alcohol and ether induces separation of the nitrate in crystalline form. Ignition or percussion explodes the dry salt with great energy, and *only a few decigrammes should be isolated in the dry state.* Almost all the dry diazonium salts are excessively explosive, and therefore must be handled with great care, but in aqueous solution they are harmless. As they yield derivatives without being isolated, they are seldom prepared in the solid state.

306. The constitution indicated for the diazonium salts is inferred from the following considerations.

The group N_2X of the diazonium compounds, X representing an acid-residue, is united with only one carbon atom of the benzene-nucleus, for all their transformations produce substances containing a group likewise attached to one carbon atom only of the nucleus.

In many respects the group $C_6H_5 \cdot N_2$— behaves like an alkali-metal, and still more like the ammonium radical. With strong mineral acids it forms colourless salts of neutral reaction, like potassium chloride and ammonium chloride, and its salts with carbonic acid resemble the alkali-metal carbonates in having an alkaline reaction due to hydrolytic dissociation. The conductivity of the diazonium salts of hydrogen chloride and other acids indicates them to be as much ionized as potassium chloride and ammonium chloride. Similarly, diazonium chlorides yield complex platinum salts soluble with difficulty in water, such as $(C_6H_5N_2Cl)_2PtCl_4$. Other analogous salts, such as $(C_6H_5N_2Cl)AuCl_3$, have been obtained also. Free *benzenediazonium hydroxide*, $C_6H_5 \cdot N_2 \cdot OH$, is known only in the form of its strongly alkaline aqueous solution. It is obtained from the aqueous solution of the chloride and silver oxide, or by the addition of the equivalent quantity of barium-hydroxide solution to the sulphate. Like potassium-hydroxide solution, it is colourless, but through decomposition it deposits gradually a flocculent resin-like substance.

The existence of a quinquivalent nitrogen atom like that in the ammonium salts must therefore be assumed in the diazonium salts, the basic properties of the members of each class being due to its presence. Two formulæ are possible:

$$C_6H_5N{\equiv}N \cdot X \quad \text{or} \quad C_6H_5N\begin{matrix} X \\ \diagup\!\!\diagdown \\ N \end{matrix}.$$

For reasons given in 308, the preference must be given to the second formula.

Benzenediazonium hydroxide is a strong base, but reacts with alkalis in a manner unknown among the strong mineral bases. Addition of a diazonium salt to a strong or dilute solution of potassium hydroxide induces separation of a potassium derivative, $C_6H_5 \cdot N_2 \cdot OK$. The molecular conductivity of a mixture of dilute solutions of benzenediazonium hydroxide and an equivalent quantity of sodium hydroxide is considerably less than the sum of the two electric conductivities of the solutions separately. A portion of the ions $(C_6H_5N_2O)' + H^{\bullet}$ and $Na^{\bullet} + OH'$ brought into contact must have changed to the non-ionized state as a result of the union of $H^{\bullet}$ and OH', a salt having been formed.

These facts indicate the strongly basic diazonium hydroxide also to have an acidic character. Such a contradictory nature being very improbable, HANTZSCH assumed the existence in the aqueous solution of an equilibrium between the diazonium hydroxide and the *syn*diazohydroxide (308):

$$\underset{\text{Diazonium hydroxide}}{\begin{array}{c} C_6H_5N \cdot OH \\ \| \\ N \end{array}} \rightleftarrows \underset{\textit{syn}\text{Diazo-hydroxide}}{\begin{array}{c} C_6H_5N \\ \| \\ HON \end{array}}.$$

He supposed the alkali-metal compounds to be derived from the *syn*-diazohydroxide.

Reactions of the Diazonium Compounds.

307. Many of the reactions of the diazonium compounds are characterized by the elimination from the molecule of the group $—N_2—$ as free nitrogen, and its replacement by a substituent united with the benzene-nucleus by a single bond. Extended research has revealed the conditions best suited for obtaining nearly quantitative results in most of these reactions.

1. *Replacement of the N_2-group by hydroxyl.*—This reaction is induced by allowing the aqueous solution of the diazonium salt to stand, or by warming it:

$$C_6H_5 \cdot N_2 \cdot Cl + HOH = C_6H_5 \cdot OH + N_2 + HCl.$$

2. *Replacement by an alkoxyl-group,* $—O \cdot C_nH_{2n+1}$.—This replacement involves boiling a diazonium salt with alcohol:

$$C_6H_5 \cdot N_2 \cdot \boxed{HSO_4 + H}\ O \cdot C_2H_5 = C_6H_5O \cdot C_2H_5 + N_2 + H_2SO_4.$$

Sometimes sunlight exerts an accelerating influence on reactions of the type described in 1 and 2.

3. *Replacement of the diazonium-group by hydrogen.*—Under certain conditions the diazonium salts do not yield alkoxyl-compounds with

alcohols, but produce the corresponding hydrogen compounds, the alcohols being converted into aldehydes:

$$\underset{\text{chloride}}{\underset{p\text{-Nitrobenzenediazonium}}{NO_2 \cdot C_6H_4 \cdot N_2 \cdot Cl}} + C_2H_5OH = \underset{\text{benzene}}{\underset{\text{Nitro-}}{NO_2 \cdot C_6H_5}} + \underset{\text{dehyde}}{\underset{\text{Acetal-}}{C_2H_4O}} + N_2 + HCl.$$

Usually reactions 2 and 3 proceed simultaneously, but with the higher alcohols replacement by hydrogen predominates for a benzene-nucleus already attached to several negative substituents, such as halogen atoms or nitro-groups.

Another method of substituting hydrogen for the amino-group is mentioned in **310.**

4. *Replacement of the diazonium-group by chlorine.*—This reaction depends on the action of a solution of diazonium chloride on either cuprous chloride dissolved in concentrated hydrochloric acid (SANDMEYER), or finely-divided copper (GATTERMANN):

$$C_6H_5 \cdot N_2 \cdot Cl = C_6H_5 \cdot Cl + N_2.$$

Cuprous chloride and finely-divided copper have a catalytic action, a copper compound probably being formed as an intermediate product, and afterwards decomposed.

The mode of replacement by bromine is similar. In the preparation of bromobenzene a solution of potassium bromide is added to an aqueous solution of benzenediazonium sulphate containing free sulphuric acid, addition of copper-dust to this mixture evolving nitrogen and forming bromobenzene.

Replacement by iodine is induced readily by adding a warm solution of potassium iodide to a diazonium-sulphate solution, it being unnecessary to employ copper or cuprous chloride.

5. *Replacement of the diazonium-group by the cyano-group.*—This replacement also is effected readily in presence of copper compounds. The solution of the diazonium salt is added to one of potassium cuprous cyanide:

$$C_6H_5 \cdot N_2 \cdot Cl + KCN = C_6H_5 \cdot CN + N_2 + KCl.$$

This reaction is of great importance for the synthesis of aromatic acids, these substances being produced by hydrolysis of the carbonitriles formed.

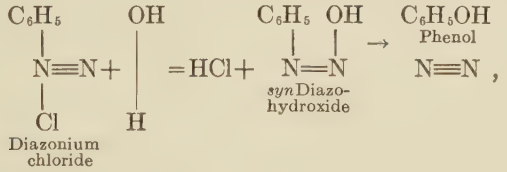
6. *Replacement of the diazonium-group by sulphur.*—Addition of a solution of potassium xanthate (**264**) to one of a diazonium salt usually precipitates the diazonium xanthate:

$$C_6H_5 \cdot N_2 \cdot Cl + KS \cdot CS \cdot OC_2H_5 = C_6H_5 \cdot N_2 \cdot S \cdot CS \cdot OC_2H_5 + KCl.$$

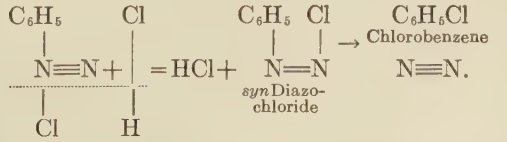
Warming the precipitate with its mother-liquor liberates nitrogen, sulphur becoming attached directly to the nucleus to form *phenyl xanthate*, $C_6H_5 \cdot S \cdot CS \cdot OC_2H_5$. The constitution of the product is indicated by its oxidation to benzenesulphonic acid. This reaction was discovered by LEUCKART, and furnishes a valuable method for the introduction of sulpho-groups into benzene derivatives at positions not accessible through the direct action of sulphuric acid.

These processes illustrate the importance of the diazonium salts as intermediate products in the preparation of numerous substances. As they are derived from amines prepared by the reduction of nitro-compounds, obviously the nitration of aromatic derivatives is a reaction of great importance, the nitro-group being replaceable at will by almost all other elements or groups through the medium of the amino-compounds and the diazonium compounds.

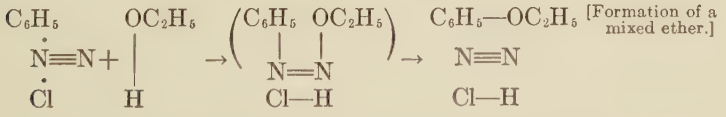
308. The reactions of the diazonium compounds can be explained by assuming them not to react directly, but to undergo preliminary conversion into *syn*diazo-compounds subsequently decomposed with evolution of nitrogen. The formation of phenol can be represented by the scheme

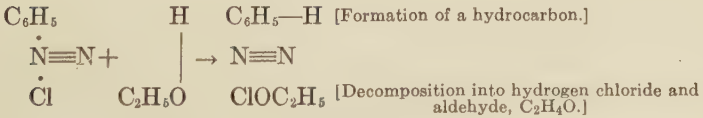


and that of chlorobenzene by the scheme



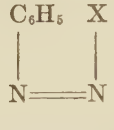
The reactions between diazonium salts and alcohol are explained by the schemes



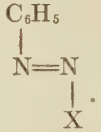


As these transformations of diazonium salts cannot be represented by the aid of the other possible structural formula, $C_6H_5 \cdot N \equiv N \cdot X$, evidently it must be rejected (306).

Most of the *syn*diazo-compounds are very unstable. They change readily into *anti*diazo-compounds assumed not to have the phenyl-group and the acid-residue contiguous, and therefore to lack the power of uniting:



*syn*Diazo-compound; C_6H_5 and X can unite



*anti*Diazo-compound; C_6H_5 and X cannot unite

With substances such as the diazocyanides HANTZSCH was able to isolate these intermediate products, thereby confirming these views. The addition of cyanides to diazotized p-*chloroaniline*, $Cl \cdot C_6H_4 \cdot NH_2$, is an example. p-*Chlorobenzonitrile*, $Cl \cdot C_6H_4 \cdot CN$, is not formed immediately; but it is possible to isolate a yellow intermediate product, $Cl \cdot C_6H_4 \cdot N_2 \cdot CN$, converted into *p*-chlorobenzonitrile by addition of copper-dust, the action being accompanied by an energetic evolution of nitrogen. This yellow intermediate p-*chlorobenzene*syn*diazocyanide* is very unstable, and speedily changes to the isomeric *anti*-compound, a substance unaffected by copper-dust. Stereochemical theory therefore affords a satisfactory explanation of the observed phenomena.

309. The importance of the diazonium compounds is not confined to reactions involving the elimination of the nitrogen atoms, for they are retained in some important derivatives.

1. *Diazoamino-compounds* are obtained by the action of primary and secondary amines on diazonium salts:

$$C_6H_5 \cdot N_2 \cdot \boxed{Cl+H} NHC_6H_5 = \underset{\text{Diazoaminobenzene}}{C_6H_5 \cdot N_2 \cdot NHC_6H_5} + HCl.$$

They are produced also by the interaction of nitrous acid and free aniline instead of an aniline salt. In this reaction benzenediazonium hydroxide or benzenediazohydroxide can be assumed to be the primary product, and instantly to react with a molecule of the aniline still present:

I. $$C_6H_5 \cdot NH_2 + HNO_2 = C_6H_5 \cdot N_2 \cdot OH + H_2O.$$

II. $$C_6H_5 \cdot N_2 \cdot \underset{\text{Benzenediazohydroxide}}{\boxed{OH+H}} NHC_6H_5 = C_6H_5 \cdot N{:}N \cdot NHC_6H_5 + H_2O.$$

The diazoamino-compounds are crystalline and have a yellow

colour. They do not unite with acids. In acid solution they are converted by nitrous acid into diazonium salts:

$$C_6H_5\cdot N:N\cdot NHC_6H_5+HNO_2+2HCl=2C_6H_5\cdot N_2\cdot Cl+2H_2O.$$

2. Diazonium salts combine with aromatic amines, especially the tertiary derivatives, to form *aminoazo-compounds* by attack on the *para*-position of the amine:

$$C_6H_5\cdot N_2Cl+H\cdot C_6H_4\cdot N(CH_3)_2=HCl+C_6H_5\cdot N{=}{=}N\cdot C_6H_4\cdot N(CH_3)_2.$$

Dimethylaniline — Dimethylaminoazobenzene

When diazoamino-compounds are heated with aniline and its hydrochloride, they yield aminoazo-compounds, diazoaminobenzene being transformed into *aminoazobenzene*, $C_6H_5\cdot N:N\cdot C_6H_4\cdot NH_2$. The first step in this process is the conversion of the diazoamino-compound into aniline and benzenediazonium chloride, the *para*-hydrogen atom of this chloride then reacting with more aniline. The accuracy of this view of the mechanism of the process is proved by substituting *m*-toluidine for aniline in the second stage, the product then being *benzeneazotoluidine:*

$$C_6H_5\cdot N_2\cdot Cl+H\cdot C_6H_3<\begin{matrix}CH_3\\NH_2\end{matrix}=HCl+C_6H_5\cdot N{=}N\cdot C_6H_3<\begin{matrix}CH_3\\NH_2\end{matrix}.$$

Benzeneazotoluidine

3. Diazonium salts react similarly with phenols, forming *hydroxyazo-compounds*. This combination requires the presence of alkalis:

$$C_6H_5\cdot N_2\cdot \boxed{Cl+H}\, C_6H_4OH=C_6H_5\cdot N:N\cdot C_6H_4OH+HCl.$$

Phenol — Hydroxyazobenzene

Important dyestuffs are derived from *hydroxyazobenzene* (341).

VIII. HYDRAZINES.

310. The typical derivative of hydrazine is *phenylhydrazine*, $C_6H_5\cdot NH\cdot NH_2$, mentioned several times in the aliphatic series in connexion with its action on aldehydes, ketones, and sugars (103, 203, and 209). It is formed by the reduction of diazonium salts such as benzenediazonium chloride by the action of the calculated quantity of stannous chloride dissolved in hydrochloric acid:

$$C_6H_5\cdot N_2\cdot Cl+4H=C_6H_5\cdot NH{-}{-}NH_2,HCl.$$

The hydrochloride, $C_6H_5\cdot NH\cdot NH_2,HCl$, separates, being soluble with difficulty in water and almost insoluble in hydrochloric acid.

Phenylhydrazine is a colourless oily liquid, and in the air turns brown. Its melting-point is 19·6°, and its boiling-point is 241°. Boiling at the ordinary pressure causes some decomposition. It is only slightly soluble in water.

Phenylhydrazine is decomposed by energetic reduction into aniline and ammonia. It is very sensitive towards oxidizers, its sulphate being converted by mercuric oxide into the diazonium salt. Usually oxidation goes further, and eliminates the nitrogen from the molecule, an alkaline copper solution converting it into water, nitrogen, and

benzene. Phenylhydrazine has a wholly basic character, and yields well-defined crystalline salts.

Phenylhydrazine is indicated to have the constitutional formula $C_6H_5 \cdot NH \cdot NH_2$ by the following reactions. A secondary amine is converted by nitrous acid into the corresponding nitrosoamine:

$$\underset{\text{Monomethylaniline}}{C_6H_5 \cdot N{<}^{H}_{CH_3}} \rightarrow \underset{\text{Nitrosomethylaniline}}{C_6H_5 \cdot N{<}^{NO}_{CH_3}}.$$

Careful reduction of this substance yields *methylphenylhydrazine*, $C_6H_5 \cdot N{<}^{NH_2}_{CH_3}$, also obtainable from phenylhydrazine by the action of sodium, one hydrogen atom being replaced by the metal. With methyl iodide this sodium compound gives the same methylphenylhydrazine:

$$C_6H_5 \cdot NH \cdot NH_2 \rightarrow C_6H_5 \cdot N{<}^{NH_2}_{Na} \rightarrow C_6H_5 \cdot N{<}^{NH_2}_{CH_3}.$$

IX. AROMATIC MONOBASIC ACIDS: BENZOIC ACID AND ITS HOMOLOGUES.

311. *Benzoic acid*, $C_6H_5 \cdot COOH$, can be prepared by many methods. The most important reactions will be described.

1. By the oxidation of any aromatic hydrocarbon with a side-chain:

$$C_6H_5 \cdot C_nH_{2n+1} \rightarrow C_6H_5 \cdot COOH.$$

Being inexpensive, toluene is specially serviceable for this purpose. In the manufacture of benzoic acid, toluene is not oxidized directly, but reacts at its boiling-point with chlorine. *Benzotrichloride*, $C_6H_5 \cdot CCl_3$, is the initial product, and is converted into benzoic acid by heating with water:

$$C_6H_5 \cdot C\begin{vmatrix} Cl & H \\ Cl & H \\ Cl & H \end{vmatrix}\begin{matrix} OH \\ OH \\ OH \end{matrix} - H_2O = C_6H_5 \cdot COOH + 3HCl.$$

Benzoic acid prepared in this way often contains traces of *chlorobenzoic acid*, $C_6H_4Cl \cdot COOH$.

2. By the oxidation of aromatic alcohols or aldehydes, such as benzyl alcohol, $C_6H_5 \cdot CH_2OH$, or benzaldehyde, $C_6H_5 \cdot C{\leqslant}^{H}_{O}$; or of alcohols, aldehydes, or ketones with longer side-chains; or of any compound containing a side-chain with one carbon atom in direct union with the benzene-nucleus.

3. By the introduction of the cyano-group into the benzene-nucleus,

and hydrolysis of the *benzonitrile*, $C_6H_5 \cdot CN$. The substitution of the cyano-group can be effected in various ways:

(*a*) By diazotizing aniline, and bringing the diazonium salt into contact with potassium cyanide (**307**, 5).

(*b*) By distilling potassium benzenesulphonate with potassium cyanide (compare **78**):

$$C_6H_5 \cdot SO_3K + KCN = C_6H_5 \cdot CN + K_2SO_3.$$

(*c*) By the interaction of cyanogen bromide and aromatic hydrocarbons in presence of aluminium chloride.

(*d*) By heating bromobenzene at 200° with an aqueous-alcoholic solution of potassium cyanide in presence of cuprous cyanide. There is simultaneous hydrolysis of the cyano-group, resulting in the immediate formation of benzoic acid.

4. By the action on benzene of various derivatives of carbonic acid, other than carbon dioxide, substances readily convertible into benzoic acid are formed:

(*a*) In presence of aluminium chloride, benzene and carbonyl chloride react to form *benzoyl chloride*, the chloride of benzoic acid, and hydrogen chloride:

$$C_6H_5\boxed{H+Cl} \cdot COCl = \underset{\text{Benzoyl chloride}}{C_6H_5 \cdot COCl} + HCl.$$

Benzoyl chloride is converted by hot water into benzoic acid.

(*b*) Benzene and aluminium chloride react with *carbamyl chloride*, $Cl \cdot CONH_2$ (formed by passing carbonyl chloride over heated ammonium chloride), yielding *benzamide*, the amide of benzoic acid:

$$C_6H_5\boxed{H+Cl} \cdot CONH_2 = \underset{\text{Benzamide}}{C_6H_5 \cdot CONH_2} + HCl.$$

(*c*) Bromobenzene is converted by sodium and ethyl chlorocarbonate into *ethyl benzoate*:

$$\begin{matrix} C_6H_5 \\ + \end{matrix}\boxed{\begin{matrix} Br+Cl \\ Na\ \ Na \end{matrix}} \cdot COOC_2H_5 = C_6H_5 \cdot COOC_2H_5 + NaCl + NaBr.$$

312. Benzoic acid is a constituent of many natural resins and balsams, such as gum-benzoin, Peru-balsam, and Tolu-balsam. A derivative termed hippuric acid (**242**) is present in the urine of horses. Formerly benzoic acid was prepared principally from gum-benzoin, and that employed as a medicament still is obtained sometimes from this source. It is a white solid crystallizing in leaf-like crystals melting at

121·4°. It sublimes readily, boils at 250°, and being volatile with steam it can be purified by steam-distillation. Its alkali-metal salts dissolve readily in water, most salts of other bases being soluble with difficulty.

The solubility-curve ("Inorganic Chemistry," 236) of benzoic acid has been the subject of careful investigation on account of its interesting character (Fig. 71). The solubility increases somewhat rapidly with rise of temperature up to 90° (*AB*). At that temperature the acid melts beneath the water, and two liquids are produced. One of them is an aqueous solution containing 11·2 per cent. of acid (point *B*); the other consists principally of the acid, containing 95·88 per cent. (point *D*). The mutual solubility of these layers is represented in the part *BCD* of the curve, *BC* corresponding with the aqueous layer, and *DC* with the acid layer. The composition of the two layers becomes more and more alike as the temperature rises, the water dissolving more benzoic acid, and the acid more water. At 116° they are identical in composition, the liquid having become homogeneous again.

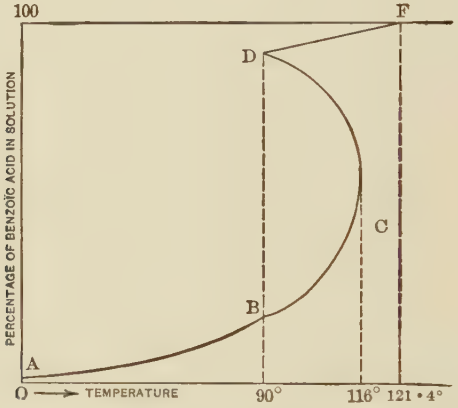


Fig. 71.—Solubility-curve of Benzoic Acid in Water.

If more benzoic acid be added to the acid layer only at 90°, it is necessary to raise the temperature to keep all the acid fused; and there is obtained the line *DF* ending at *F*, the melting-point of pure benzoic acid or 121·4°. *DF* therefore represents the melting-point-curve of the acid corresponding with the addition of increasing amounts of water.

Derivatives of Benzoic Acid.

313. *Benzoyl chloride*, $C_6H_5 \cdot COCl$, can be obtained by the action of phosphorus pentachloride or oxychloride on benzoic acid, or by the method of 311, 4*a*. It is a liquid of disagreeable odour, and boils at 194°. It is manufactured by the interaction of chlorine and benzalde-

hyde, $C_6H_5 \cdot C\overset{H}{\underset{O}{}}$. It reacts with water very slowly at the ordinary temperature, a difference from acetyl chloride.

Benzoyl chloride is employed in the introduction of the benzoyl-group, $C_6H_5 \cdot CO—$, into compounds. This operation is effected by a method discovered by BAUMANN and SCHOTTEN, involving agitation of the substance in alkaline solution with benzoyl chloride.

Amines are benzoylated readily by suspending their hydrochlorides in benzene, adding the equivalent quantity of benzoyl chloride, and heating until evolution of hydrogen chloride has ceased.

Benzoic anhydride, $C_6H_5CO \cdot O \cdot COC_6H_5$, is formed by the interaction of a benzoate and benzoyl chloride:

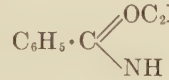
$$C_6H_5 \cdot CO \cdot O\boxed{Na+Cl} \cdot OCC_6H_5 = NaCl + C_6H_5CO \cdot O \cdot COC_6H_5.$$

At the ordinary temperature it is very stable towards water, but the boiling liquid decomposes it so as to generate benzoic acid.

Sometimes the formation of *ethyl benzoate* (**311**, 4*c*) is employed as a test for ethyl alcohol, as it possesses a characteristic peppermint-like odour.

Benzamide (**311**, 4*b*), $C_6H_5 \cdot CONH_2$, can be prepared by the action of ammonia or ammonium carbonate on benzoyl chloride. It is crystalline and dimorphous, melting at 130°. In **96** the influence of the negative acetyl-group is stated to cause the hydrogen atoms of the amino-group in acetamide to be replaceable by metals. Benzamide displays this property to an even greater extent, on account of the more negative character of the benzoyl-group; for the value of the dissociation-constant for acetic acid is $10^4k = 0 \cdot 18$, and that for benzoic acid is $10^4k = 0 \cdot 60$.

The silver compound of benzamide reacts with an alkyl iodide at the ordinary temperature to form the *O*-ether *benzoic iminoether*,



The constitution of this substance is proved by its conversion by alkalis into ammonia and alcohol, instead of into ethylamine and benzoic acid. In contrast, contact of the silver compound with an alkyl iodide at 100° yields the *N*-alkide , the course of the reaction being indicated by the decomposition of the *N*-alkide into ethylamine and benzoic acid.

Benzonitrile, $C_6H_5 \cdot CN$, is produced by methods described in **311**, 3, and also can be prepared similarly to the aliphatic nitriles, as by the action of phosphoric oxide on benzamide. It is a liquid with an odour resembling that of bitter almonds, and boils at 191°. It has all the properties characteristic of the aliphatic nitriles.

The *homologues of benzoic acid* such as the *toluic acids*,

$$CH_3 \cdot C_6H_4 \cdot COOH,$$

and the *xylic acids*, $(CH_3)_2C_6H_3 \cdot COOH$, are crystalline solids very slightly soluble in water. They are prepared by methods analogous to those employed for benzoic acid.

X. AROMATIC ALDEHYDES AND KETONES.

Aldehydes.

314. *Benzaldehyde*, $C_6H_5 \cdot C\overset{H}{O}$, is the best-known of the aromatic aldehydes. Like the aliphatic aldehydes, it is formed by the oxidation of the corresponding benzyl alcohol, $C_6H_5 \cdot CH_2OH$, and by the distillation of a mixture of a benzoate and a formate. It is manufactured by heating *benzal chloride*, $C_6H_5 \cdot CHCl_2$, with water and calcium carbonate, a method whose aliphatic analogue is without practical importance:

$$C_6H_5 \cdot CH\boxed{Cl_2 + \begin{matrix}H\\H\end{matrix}}\begin{matrix}OH\\OH\end{matrix} - H_2O = C_6H_5 \cdot C\overset{H}{O} + 2HCl.$$

Another method for the technical preparation of benzaldehyde involves direct oxidation of toluene with manganese dioxide and sulphuric acid in presence of a small proportion of cupric sulphate as catalyst.

The following methods are employed in the preparation of the homologues of benzaldehyde:

1. When ethyl chloro-oxalate is brought into contact with an aromatic hydrocarbon in presence of aluminium chloride, the ethyl ester of a 1-ketonic acid is produced:

$$C_6H_6 + ClCO{-}COOC_2H_5 = C_6H_5 \cdot CO \cdot COOC_2H_5 + HCl.$$

Ethyl chloro-oxalate

The free acid is obtained by saponification, and dry distillation expels carbon dioxide to form the aldehyde:

$$C_6H_5 \cdot CO \cdot CO_2H = C_6H_5 \cdot C\overset{H}{O} + CO_2.$$

2. An aromatic hydrocarbon and a mixture of carbon monoxide and

hydrogen chloride react in presence of aluminium chloride and a trace of cuprous chloride. Formyl chloride, HCOCl, can be assumed to be an intermediate product:

$$CH_3 \cdot C_6H_5 + ClOCH = CH_3 \cdot C_6H_4 \cdot C\begin{matrix}H\\O\end{matrix} + HCl.$$

315. Benzaldehyde occurs in the natural product amygdaloside, $C_{20}H_{27}O_{11}N$ (256), and on this account it is termed *oil of bitter almonds.* It is a liquid of agreeable odour, is slightly soluble in water, boils at 179°, and at 15° has the density 1·0504. It has most of the properties of the aliphatic aldehydes, being oxidized readily even by the oxygen of the atmosphere, especially under the influence of sunlight. It also reduces an ammoniacal silver solution with formation of a mirror, yields a crystalline addition-product with sodium hydrogen sulphite, adds hydrogen cyanide and hydrogen, forms an oxime and a phenylhydrazone, and so on.

It displays, however, points of difference from the fatty aldehydes. An example is the inability of ammonia at the ordinary temperature to yield a compound like acetaldehydeammonia, *hydrobenzamide,* $(C_6H_5CH)_3N_2$, being formed by the union of three molecules of benzaldehyde and two molecules of ammonia:

$$3C_6H_5 \cdot C\begin{matrix}H\\O\end{matrix} + 2H_3N = (C_6H_5CH)_3N_2 + 3H_2O.$$

At −20° ammonia does combine with benzaldehyde to *benzaldehydeammonia,* $2C_6H_5 \cdot CHO,NH_3$, its structure probably being

$$NH[CH(C_6H_5) \cdot OH]_2.$$

This derivative separates in plates melting at 45°. After the lapse of some time it decomposes into hydrobenzamide, benzaldehyde, and water. It is an intermediate product in the preparation of hydrobenzamide.

The behaviour of the aromatic aldehydes towards alcoholic potassium hydroxide is characteristic, and conforms with CANNIZZARO's reaction (108), benzaldehyde yielding potassium benzoate and benzyl alcohol:

$$2C_6H_5 \cdot C\begin{matrix}H\\O\end{matrix} + KOH = C_6H_5 \cdot COOK + C_6H_5 \cdot CH_2OH.$$

The aromatic aldehydes condense readily with dimethylaniline and with phenols to form derivatives of triphenylmethane (373):

$$\begin{matrix} & H & \\ C_6H_5 \cdot C & O & \begin{matrix}H\\H\end{matrix} \end{matrix} \begin{matrix}C_6H_4OH\\C_6H_4OH\end{matrix} = C_6H_5 \cdot CH < \begin{matrix}C_6H_4OH\\C_6H_4OH\end{matrix} + H_2O.$$

Benzaldehyde also reacts very readily with aniline. Gentle heating of a mixture of equal volumes of the two substances causes the separation of drops of water, cooling being attended by crystallization of *benzylideneaniline,* $C_6H_5 \cdot CH{:}N \cdot C_6H_5$, melting at 45°.

The action of chlorine on benzaldehyde is described in 313.

Benzaldehydephenylhydrazone, $C_6H_5 \cdot CH:N \cdot NH \cdot C_6H_5$, is precipitated very readily by the addition of benzaldehyde drop by drop to a sulphurous-acid solution of phenylhydrazine, the reaction being accompanied by the evolution of considerable heat. It forms pale-yellow crystals melting at 152°, and is transformed by the action of violet or ultraviolet light into a scarlet-red isomeride, the original colour being restored by exposure to yellow or green light.

Autoxidation.

During the oxidation of various substances in the air as much oxygen is rendered "active" as that utilized by the substance under oxidation, a phenomenon displayed in the atmospheric oxidation of benzaldehyde. If it be kept for several weeks in contact with water, indigosulphonic acid, and air, the same amount of oxygen is absorbed in oxidizing the indigo derivative as in converting the benzaldehyde into benzoic acid. von Baeyer proved benzoyl-hydrogen peroxide, $C_6H_5CO \cdot O \cdot OH$, to be formed as an intermediate product, and to oxidize the indigosulphonic acid, the peroxide being reduced to benzoic acid:

$$C_6H_5 \cdot CHO + O_2 = C_6H_5 \cdot CO \cdot O \cdot OH;$$

$$C_6H_5 \cdot CO \cdot O \cdot OH + \text{Indigo} = C_6H_5 \cdot COOH + \text{Oxidized indigo}.$$

The oxidation of benzaldehyde in the air must accord with the equations

$$C_6H_5 \cdot CHO + O_2 = C_6H_5 \cdot CO \cdot O \cdot OH;$$

$$C_6H_5 \cdot CO \cdot O \cdot OH + C_6H_5 \cdot CHO = 2C_6H_5 \cdot COOH.$$

von Baeyer demonstrated the solubility of benzoyl-hydrogen peroxide in benzaldehyde, but noted the gradual solidification of the liquid to pure benzoic acid.

The oxidation of benzaldehyde is very much retarded by the presence of even such a small proportion of quinol as one part in a thousand, and other phenols such as catechol and pyrogallol exert a similar influence. This phenomenon is not limited to the oxidation of benzaldehyde; for the oxidation of other aldehydes, and also of such substances as oil of linseed and oil of turpentine, is strongly retarded by the presence of small proportions of the phenols cited. These remarkable phenomena were discovered by Moureu and Dufraisse, and they termed substances capable of decelerating oxidation "Antioxygens." In addition to phenols certain other materials can exert an antioxygenic effect in some instances, an example being sodium iodide.

Ketones.

316. The *aromatic ketones* can be subdivided into the mixed aromatic-aliphatic ketones and the true aromatic ketones. The typical member of the first class is *acetophenone*, $C_6H_5 \cdot CO \cdot CH_3$. It can be obtained by leading a mixture of the vapours of acetic acid and benzoic acid over thorium oxide, ThO_2, at temperatures between 430° and 460°; or more readily by the addition of aluminium chloride to a mixture of

benzene and acetyl chloride. It is a crystalline substance of agreeable odour, melts at 20°, and boils at 200°. It is slightly soluble in water, and possesses all the properties of the aliphatic ketones. It is employed as a soporific under the name "hypnone."

Benzophenone, $C_6H_5 \cdot CO \cdot C_6H_5$, is a true aromatic ketone, and is produced by the dry distillation of calcium benzoate, and by the action of benzene and aluminium chloride on benzoyl chloride or carbonyl chloride. This compound is a true aromatic derivative, but it behaves exactly like an aliphatic ketone, for its reduction yields *benzhydrol*, $C_6H_5 \cdot CHOH \cdot C_6H_5$, and *benzpinacol*, $\begin{matrix}(C_6H_5)_2C & \text{——} & C(C_6H_5)_2 \\ \dot{O}H & & \dot{O}H\end{matrix}$ (150).

Fusion of benzophenone with potassium hydroxide gives benzene and potassium benzoate:

$$C_6H_5 \cdot CO \cdot C_6H_5 + KOH = C_6H_6 + C_6H_5 \cdot COOK.$$

317. Benzophenone exists in an unstable modification melting at 27°, and in a stable form melting at 49°.

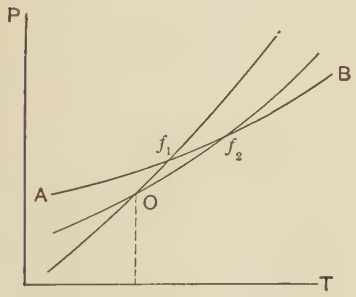


FIG. 72.—ENANTIOTROPIC SUBSTANCE.

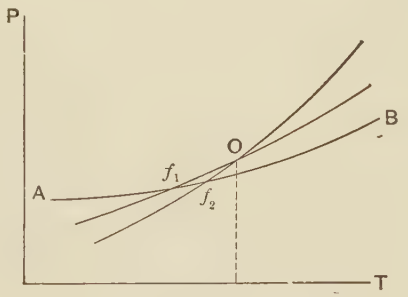


FIG. 73.—MONOTROPIC SUBSTANCE.

The relationship of these substances is one of *monotropy*, the metastable modification at all temperatures up to its melting-point changing to the stable from, but the process not being reversible. The explanation lies in the fact of the transition-point of the two modifications being higher than the melting-point of the metastable isomeride.

For a substance with a transition-point O the vapour-pressure P in the neighbourhood of this point is represented by Fig. 72 ("Inorganic Chemistry," 70). AB is the vapour-pressure curve of the fused substance. Its direction must be such as to be lower on the right than any other curve, and therefore to be nearest to the horizontal axis. As rise of temperature ultimately occasions the fusion of all solid forms, above a temperature definite for each substance the liquid phase must be the more stable, and therefore have the lower vapour-pressure. Of_1 is the melting-point of the

metastable modification, a temperature higher than the transition-point; and Of_2 is that of the stable modification.

AB can be situated so as to place f_1 and f_2 below O (Fig. 73). The melting-point in this instance being lower than the transition-point O, the transformation cannot be attained. Under such conditions the metastable modification remains in the metastable state up to its melting-point, the substance being *monotropic*. In the more usual phase of *enantiotropy*, rise of temperature causes the compound to attain the transition-point, then to undergo transformation, and finally to melt.

Oximes.

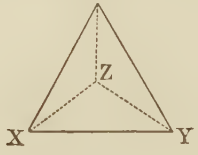
318. Some of the *oximes* of the aromatic aldehydes and ketones exhibit a peculiar kind of isomerism. There are two isomerides of benzaldoxime, *benz*anti*aldoxime* (α) melting at 35°, and *benz*syn*aldoxime* (β or *iso*) melting at 128°. With acetic anhydride the β-form readily loses water to yield benzonitrile:

$$\begin{matrix} C_6H_5C\,H \\ \|\;\;| \\ N\;OH \end{matrix} = C_6H_5\cdot C{\equiv}N + H_2O.$$

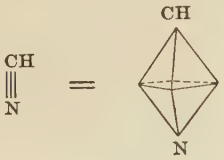
Acetic anhydride converts the *anti*aldoxime into an acetyl-derivative.

Isomerides of the ketoximes $\begin{matrix} R \\ R' \end{matrix}\!>\!C\!:\!NOH$ with R and R′ similar do not exist, but for dissimilar groups two isomerides are known. Benzophenoneoxime and its derivatives furnish examples. Despite many attempts to prepare an isomeride, benzophenoneoxime is known in one modification only; but after substitution of hydrogen in one phenyl-group two isomeric oximes can be obtained. The substances *monochlorobenzophenone*, $C_6H_5\cdot CO\cdot C_6H_4Cl$, *monobromobenzophenone*, $C_6H_5\cdot CO\cdot C_6H_4Br$, *phenyltolylketone*, $CH_3\cdot C_6H_4\cdot CO\cdot C_6H_5$, and *phenylanisylketone*, $CH_3O\cdot C_6H_4\cdot CO\cdot C_6H_5$, are examples of ketones yielding two isomeric oximes. Many other compounds of this type could be cited.

After several ineffectual attempts to explain such isomerism by the ordinary structural formulæ, the following stereochemical explanation of the observed facts was adopted. The three affinities of the nitrogen atom are assumed to be directed towards the angles of a tetrahedron, the nitrogen atom being situated at the fourth angle:

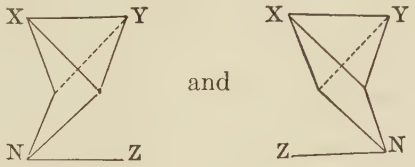


With the three nitrogen bonds attached to carbon, as in the carbonitriles, the following spacial representation is obtained:



In this instance stereoisomerism is impossible, and experience has proved none of the numerous known nitriles to have two forms due to isomerism in the cyano-groups.

With the nitrogen atom attached to carbon by two bonds, two isomeric forms become possible:



These formulæ can be represented more readily by

$$\begin{matrix} X{-}C{-}Y \\ \| \\ N{-}Z \end{matrix} \quad \text{and} \quad \begin{matrix} X{-}C{-}Y \\ \| \\ Z{-}N \end{matrix} .$$

Obviously different configurations for such compounds are obtained only when X and Y are different, for when they are similar the figures become identical. This view agrees with the facts stated at the beginning of this section.

XI. AROMATIC PHOSPHORUS AND ARSENIC DERIVATIVES.

319. There are known compounds of phosphorus and arsenic with aromatic hydrocarbons, having constituents similar to those of the nitro-compounds, azo-compounds, and amino-compounds.

Phosphinobenzene, $C_6H_5 \cdot PO_2$, cannot be obtained analogously to nitrobenzene, by the interaction of metaphosphoric acid and benzene. It is prepared by the action of *phenylphosphinic acid* (**72**) on its chloride:

$$\underset{\text{Phenylphosphinic acid}}{C_6H_5 \cdot PO(OH)_2} + \underset{\text{Phenylphosphinyl chloride}}{C_6H_5 \cdot POCl_2} = 2C_6H_5 \cdot PO_2 + 2HCl.$$

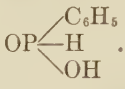
It is a white, crystalline, odourless powder.

Phenylphosphine, $C_6H_5 \cdot PH_2$, is obtained by distilling *phosphenyl chloride*, $C_6H_5 \cdot PCl_2$, with alcohol in a current of carbon dioxide. It is a liquid of very penetrating odour. It cannot be obtained by the reduction of phosphinobenzene.

Phosphobenzene, $C_6H_5 \cdot P \cdot P \cdot C_6H_5$, is got by the action of phenylphosphine on phosphenyl chloride:

$$C_6H_5 \cdot P\boxed{Cl_2+H_2}P \cdot C_6H_5 = C_6H_5 \cdot P : P \cdot C_6H_5 + 2HCl.$$

It is a pale-yellow powder, insoluble in water, alcohol, and ether. It is oxidized energetically by weak nitric acid, forming *phosphenylous acid*,



Phosphenyl chloride, $C_6H_5 \cdot PCl_2$, the starting-point in the preparation of these and other aromatic phosphorus derivatives, and its homologues can be prepared by heating aromatic hydrocarbons with phosphorus trichloride and aluminium chloride under a reflux-condenser.

Arsinobenzene, $C_6H_5 \cdot AsO_2$, is obtained by the elimination of water from *phenylarsinic acid*, $C_6H_5 \cdot AsO(OH)_2$, under the influence of heat.

Arsenobenzene, $C_6H_5 \cdot As : As \cdot C_6H_5$, is formed by the reduction of *phenylarsine oxide*, $C_6H_5 \cdot AsO$, with phosphorous acid. It forms yellow needles, and is converted by oxidation into phenylarsinic acid, $C_6H_5 \cdot AsO(OH)_2$.

Other aromatic arsenic derivatives are mentioned in **339**.

The following series of compounds are known:

$C_6H_5 \cdot NO_2$ Nitrobenzene	$C_6H_5 \cdot N_2 \cdot C_6H_5$ Azobenzene	$C_6H_5 \cdot NH_2$ Phenylamine
$C_6H_5 \cdot PO_2$ Phosphinobenzene	$C_6H_5 \cdot P_2 \cdot C_6H_5$ Phosphobenzene	$C_6H_5 \cdot PH_2$ Phenylphosphine
$C_6H_5 \cdot AsO_2$ Arsinobenzene	$C_6H_5 \cdot As_2 \cdot C_6H_5$ Arsenobenzene	—

Although these compounds have analogous formulæ, both the methods employed in the preparation of the individual members of each series, and the properties of the individuals, exhibit wide divergences.

XII. AROMATIC METALLIC COMPOUNDS.

320. Mercury, tin, lead, and magnesium are the only metals capable of yielding aromatic compounds; and they are much less important than the metallic compounds of the aliphatic series. *Mercury phenide*, $Hg(C_6H_5)_2$, is obtained by the action of sodium-amalgam on bromobenzene. It is crystalline, and resembles the corresponding alkyl-derivatives in its stability towards atmospheric oxygen. Passage of its vapour through a red-hot tube decomposes it into mercury and diphenyl (**371**), and a similar partial effect is produced by distillation.

Heating mercury acetate with benzene at 110° produces *phenylmercury acetate*, $C_6H_5 \cdot Hg \cdot OOC \cdot CH_3$, the acetic-acid salt of the base *phenylmercury hydroxide*, $C_6H_5 \cdot Hg \cdot OH$. The homologues of benzene, nitrobenzene, and other substances yield analogous compounds.

Aromatic magnesium compounds are mentioned in **289**.

BENZENE HOMOLOGUES WITH SUBSTITUTED SIDE-CHAINS.

321. The introduction of a substituent into a homologue of benzene is possible in the nucleus or in the side-chain. The second type of substitution has been investigated exhaustively for the toluene derivatives with hydrogen of the methyl-group replaced by various substituents. These substances are to be regarded as methane with one hydrogen atom replaced by phenyl, and one or more of the other hydrogen atoms exchanged for a corresponding number of atoms or radicals. A close approximation between the properties of these compounds and those of the corresponding aliphatic derivatives is to be anticipated, a view finding abundant confirmation in the facts recorded in this chapter.

I. COMPOUNDS WITH HALOGEN IN THE SIDE-CHAIN.

In the interaction of chlorine or bromine and toluene, the entrance of the halogen into the nucleus or into the side-chain is determined by the experimental conditions. Compounds of the type $X \cdot C_6H_4 \cdot CH_3$ are designated *halogen-toluenes*, and those of the formula $C_6H_5 \cdot CH_2X$ *benzyl halides*. A summary of the influence exerted by the experimental conditions is subjoined.

1. *Temperature.*—At low temperatures, halogens substitute in the nucleus; and at high temperatures, they enter the side-chain. This phenomenon is exemplified by the conversion of cold toluene by chlorine into o-*chlorotoluene* and p-*chlorotoluene*; and also by the action of chlorine or bromine on boiling toluene (110°) to produce *benzyl chloride*, $C_6H_5 \cdot CH_2Cl$, or *benzyl bromide*, $C_6H_5 \cdot CH_2Br$, almost exclusively.

2. *Sunlight.*—A striking example of the influence of light is furnished by the dark-brown mixture of toluene and bromine. At the ordinary temperature in absence of light, interaction is very slow, an interval of many days being necessary for the complete disappearance of the bromine, and the formation of hydrogen bromide and bromotoluenes. Exposure of the mixture to daylight induces decolorization in a few minutes, the bromine entering the side-chain only.

Many instances of the influence of light on chemical reactions have been observed. They include the intramolecular rearrangement of atoms and groups; the acceleration of reactions; and, as in the example

cited, the formation of compounds entirely different from those formed in absence of light.

3. *Concentration.*—The proportion of halogen to toluene has an important influence. At 50° in absence of light, the product obtained by the interaction of bromine and toluene in the molecular ratio 1:4·26 contains 24·1 per cent. of benzyl bromide, but in the ratio 1:28·55 it has 95·3 per cent. of this substance.

4. *Catalysts.*—Aluminium or ferric halides have a very powerful catalytic action. So small a proportion of ferric bromide as 0·002 gramme-molecule to each gramme-molecule of bromine completely annuls all other influences, and causes substitution in the nucleus only, the course of the reaction being unaffected by the presence of light, by high temperature, and by variation in the concentration.

The benzyl halides, $C_6H_5 \cdot CH_2X$, are readily distinguishable from the isomeric halogen derivatives of toluene. In the first place, their halogen atoms display the same aptitude for reactions involving double decomposition as those of the alkyl halides, but the halogen atoms of the isomeric halogen-toluenes are as firmly attached as those in the monohalogen-benzenes. In the second place, the benzyl halides are converted by oxidation into benzoic acid, $C_6H_5 \cdot COOH$, but the halogen-toluenes yield halogen-benzoic acids, $C_6H_4X \cdot COOH$. In the third place, the halogen-toluenes are characterized by their faint, but not disagreeable, odour; but the benzyl halides have a most irritating effect on the mucous membrane of the eyes, a property specially noticeable in benzyl iodide.

Benzyl chloride is a colourless liquid of stupefying odour intensified by warming. It boils at 178°, and at 15° has the density 1·113. *Benzyl bromide* also is a colourless liquid. *Benzyl iodide* is prepared by heating benzyl chloride with potassium iodide, melts at 24°, and is decomposed by boiling. It has a powerful and unbearably irritating odour productive of tears, and was employed for filling lachrymatory shells in the great European war.

The prolonged action of chlorine on boiling toluene yields *benzal chloride*, $C_6H_5 \cdot CHCl_2$, and *benzotrichloride*, $C_6H_5 \cdot CCl_3$.

II. PHENYLNITROMETHANE AND THE *PSEUDO*-ACIDS.

322. *Phenylnitromethane*, $C_6H_5 \cdot CH_2NO_2$, is an aromatic compound with a nitro-group in the side-chain, as is evident from its formation by the action of benzyl chloride or iodide on silver nitrite:

$$C_6H_5 \cdot CH_2\boxed{Cl+Ag}NO_2 = C_6H_5 \cdot CH_2NO_2 + AgCl.$$

It can be reduced to benzylamine, proving it to be a true nitro-compound. Phenylnitromethane, and its derivatives with substituents attached to the nucleus, exist in two tautomeric modifications readily transformed into each other. Phenylnitromethane is a liquid, and its aqueous solution does not react with ferric chloride. After conversion into its sodium derivative by the action of sodium alkoxide, addition of excess of a strong mineral acid causes the separation of a crystalline substance of the same composition as phenylnitromethane, but its aqueous solution gives a coloration with ferric chloride. After the lapse of some hours, these crystals will have become reconverted completely into the ordinary liquid phenylnitromethane. Probably the sodium compound and the unstable modification corresponding with it have the constitutions

$$C_6H_5\cdot CH{:}NO\cdot ONa \quad \text{and} \quad C_6H_5\cdot CH{:}NO\cdot OH.$$

The presence of a hydroxyl-group is indicated by the formation of *dibenzhydroxamic acid* through the agency of benzoyl chloride:

$$C_6H_5\cdot CH{:}N\begin{matrix}O\\ \diagdown\\ \diagup\\ ONa\end{matrix} + ClOC\cdot C_6H_5 \rightarrow C_6H_5\cdot CH{:}N\begin{matrix}O\\ \diagdown\\ \diagup\\ O\cdot OC\cdot C_6H_5\end{matrix} \rightarrow$$

Sodiophenyl*iso*-nitromethane

$$\rightarrow C_6H_5\cdot CO{-}\underset{H}{N}{-}O\cdot OC\cdot C_6H_5.$$

Dibenzhydroxamic acid

*iso*Nitro-compounds differ from ordinary nitro-compounds in reacting vigorously with phenyl *iso*cyanate at low temperatures, another indication of the presence of a hydroxyl-group.

These facts show the conversion of phenylnitromethane, $C_6H_5\cdot CH_2NO_2$, into a salt to be preceded by the formation of an isomeric modification. Inversely, liberation from its sodium compound produces first the *iso*-modification or *aci*-modification, it changing slowly to the ordinary form.

The dilute aqueous solution of m-*nitrophenylnitromethane* affords a striking example of this phenomenon. This compound is colourless, but its sodium salt has a deep-yellow colour. The addition of an equivalent quantity of hydrogen chloride to its deeply-tinted solution causes the yellow colour to disappear somewhat slowly, indicating the conversion of the *iso*-compound into its normal isomeride.

The discharge of the colour is attended by another phenomenon, the electric conductivity of the liquid being considerably greater immediately after the addition of the hydrogen chloride than some minutes later, when the colour has nearly vanished. The explanation lies in the *iso*-form being a true acid, and therefore a conductor in aqueous solution, the solution of the normal modification being a non-conductor, and therefore not possessing an acidic character.

The formation of an *aci*-modification is characteristic of various compounds, notably the nitroparaffins, pyrazolones, oximes, and nitrophenols.

323. Besides the properties indicated, the *pseudo*-acids possess others available for their detection. As stated, the addition of a strong acid to a *pseudo*-acid salt liberates the *aci*-form, and it is converted slowly into the normal modification. Inversely, the addition of an equivalent quantity of caustic alkali to the normal modification causes its gradual neutralization. This "slow neutralization" is a characteristic of the *pseudo*-acids.

Another of their distinctive peculiarities is illustrated by the liberation of *dinitroethane* from its sodium salt in accordance with the equation

$$CH_3\cdot C\begin{cases}NO_2\\NO\cdot ONa\end{cases} + HCl = \underset{\textit{aci}\text{-Dinitroethane}}{CH_3\cdot C\begin{cases}NO_2\\NO\cdot OH\end{cases}} + NaCl,$$

and its subsequent rapid conversion into the normal compound,

$$CH_3\cdot CH<\begin{matrix}NO_2\\NO_2\end{matrix},$$

a change in the electric conductivity of the solution being scarcely observable even at 0°. The neutral reaction of the alkali-metal derivatives of the non-conducting or weakly-conducting hydrogen compound nevertheless indicates the existence of a *pseudo*-acid. An acid so weak as to be in solution a bad conductor of electricity yields alkali-metal salts subject to extensive hydrolytic dissociation, and therefore with a strongly alkaline reaction ("Inorganic Chemistry," **66**). Such a substance as sodiodinitroethane forms a non-alkaline solution, and therefore must be derived from an acid other than dinitroethane, for this substance has a neutral reaction and in aqueous solution is a non-conductor.

The difference in structure between the salt of a *pseudo*-acid and the free acid can be detected also by refraction. Comparison of the molecular refraction of an aqueous or alcoholic solution of an acid with that of its sodium salt reveals a constant difference, even for weak acids. For a solution in the equivalent quantity of caustic alkali of a nitro-compound capable of yielding a *pseudo*-acid, the difference between the molecular refraction of the acid and that of the salt formed is much greater. This phenomenon indicates the transformation of the *pseudo*-acid into its *aci*-form to be an intermediate process preceding the formation of the salt.

The formation of such *aci*-forms has been observed for various types of compounds, the chief being nitroalkanes, nitroacetone, alkylnitrolic acids, nitrosoamines, oxyazo-compounds, pyrazolones, oximes, and nitrophenols.

III. ACIDS WITH CARBOXYL IN THE SIDE-CHAIN.

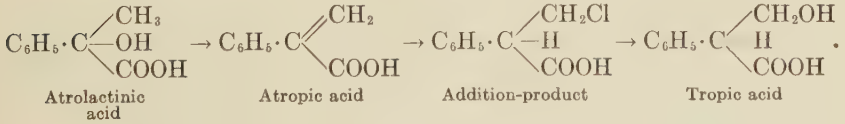
324. One of the compounds with a saturated side-chain is *phenylacetic acid*, $C_6H_5 \cdot CH_2 \cdot COOH$. It is prepared by the interaction of potassium cyanide and benzyl chloride, followed by hydrolysis of the *benzyl cyanide*, $C_6H_5 \cdot CH_2 \cdot CN$. Phenylacetic acid melts at 76°, and is converted by oxidation into benzoic acid; but the isomeric toluic acids, $C_6H_4 < \begin{matrix} CH_3 \\ COOH \end{matrix}$, are transformed by oxidation into the dibasic phthalic acids.

Mandelic acid has both hydroxyl and carboxyl in the side-chain. Its constitution is $C_6H_5 \cdot CHOH \cdot COOH$, as its synthesis from benzaldehyde and hydrogen cyanide indicates. In this reaction *mandelonitrile*, $C_6H_5 \cdot CHOH \cdot CN$, is an intermediate product. Addition of quinine to the mixture of benzaldehyde and hydrogen cyanide renders the synthesis asymmetric, an optically active mandelonitrile being formed. The quinine operates as an optically active catalyst, its effect being similar to that exerted by the enzyme emulsin. The mandelic acid found in nature is lævorotatory. The synthetic acid can be resolved by the action of cultures obtained from mildew (*Penicillium glaucum*), the dextrorotatory acid being left intact. The decomposition is attained also by the formation of the cinchonine salts, that of the dextrorotatory acid crystallizing first.

Inactive mandelic acid is termed also "para-mandelic acid." It melts at 119°, and dissolves very readily in water. The optically active modification melts at 134°, and is less soluble in water.

Tropic acid is one of the parent substances of atropine (**411**).

The synthesis of tropic acid involves the condensation of acetophenone with hydrogen cyanide, and the hydrolysis to *atrolactinic acid* of the carbonitrile formed. Dry distillation eliminates one molecule of water from atrolactinic acid and forms *atropic acid*, one molecule of hydrogen chloride being added to this substance through the influence of a concentrated solution of this halogen acid. Boiling with a dilute solution of sodium carbonate converts this addition-product into tropic acid:



IV. AROMATIC ALCOHOLS.

325. *Benzyl alcohol*, $C_6H_5 \cdot CH_2OH$, is the typical aromatic alcohol, and possesses nearly all the properties of an aliphatic alcohol. It can be obtained by the interaction of benzyl chloride and potassium acetate, and saponification of the ester of acetic acid formed. It can be prepared also by the electro-reduction of benzoic acid in sulphuric-acid solution with lead cathodes. It reacts readily with phosphorus pentachloride, yielding benzyl chloride; and it forms esters, ethers, and other derivatives. Being a primary alcohol, it can be oxidized to the corresponding aldehyde, benzaldehyde (**314**), and also to benzoic acid (**312**). It differs from the aliphatic alcohols in being resinified by sulphuric acid, and not converted into the corresponding sulphuric ester. Benzyl alcohol lacks phenolic properties; for it is insoluble in alkalis, and with ferric chloride it does not yield the characteristic phenol coloration.

Benzyl alcohol is a liquid soluble in water with difficulty. It boils at 206°, and possesses only a faint odour.

2-*Phenylethanol*-1 or *phenylethyl alcohol*, $C_6H_5 \cdot CH_2 \cdot CH_2OH$, can be obtained by the reduction of ethyl phenylacetate, $C_6H_5 \cdot CH_2 \cdot COOC_2H_5$, by sodium and ethanol (**91**). It is a colourless liquid, and at a pressure of 25 mm. boils at 117°. It has a faint, rose-like smell, and when mixed with essential oils it augments their odour and renders it permanent. On that account this alcohol is employed in the perfume industry. Essential oil of roses contains 60 per cent of it.

V. COMPOUNDS WITH THE AMINO-GROUP IN THE SIDE-CHAIN

326. *Benzylamine*, $C_6H_5 \cdot CH_2 \cdot NH_2$, is a type of the amines with the amino-group in the side-chain. It can be obtained by the various methods employed in the preparation of aliphatic amines, such as the action of benzyl chloride on ammonia, *dibenzylamine* and *tribenzylamine* also being formed; the addition of hydrogen to benzonitrile, $C_6H_5 \cdot CN$; and the reduction of phenylnitromethane, $C_6H_5 \cdot CH_2 \cdot NO_2$. The method for its formation and its properties prove benzylamine to belong to the primary amines of the aliphatic series; for it does not yield diazonium compounds; and its aqueous solution has a strongly alkaline reaction, indicating it to be a much stronger base than aniline, a substance with its amino-group under the direct influence of the phenyl-group.

Benzylamine is a liquid of ammoniacal odour. It boils at 185°, is volatile with steam, and at 19° has the density 0·93. It absorbs carbon dioxide from the air.

COMPOUNDS WITH AN UNSATURATED SIDE-CHAIN.

Hydrocarbons.

327. *Styrene* or *phenylethylene*, $C_6H_5 \cdot CH : CH_2$, derives its name from its presence in storax, an exudation from trees of *Liquidambar orientalis*. The hydrocarbon can be obtained by heating cinnamic acid (**328**),

$$C_6H_5 \cdot CH : CH \cdot CO_2H,$$

carbon dioxide being eliminated. It is a liquid of agreeable odour, and boils at 146°. Heating converts it into a vitreous mass termed *metastyrene*, a polymeride of unknown molecular weight, the same transformation proceeding slowly at the ordinary temperature. Like other substances with a double bond, styrene has the power of forming addition-products. With nitric acid it yields *nitrostyrene*, $C_6H_5 \cdot CH : CH \cdot NO_2$, its nitro-group being in the side-chain. The constitution of this compound follows from its formation by the condensation of benzaldehyde with nitromethane, under the catalytic influence of alcoholic potassium hydroxide:

$$C_6H_5 \cdot C\overset{H}{\boxed{O+H_2}}CH \cdot NO_2 = C_6H_5 \cdot CH : CH \cdot NO_2 + H_2O.$$

Phenylacetylene, $C_6H_5 \cdot C \equiv CH$, can be obtained by the interaction of acetophenone and phosphorus pentachloride to form a derivative,

$$C_6H_5 \cdot CCl_2 \cdot CH_3,$$

convertible into the hydrocarbon by potassium hydroxide; or from phenylpropiolic acid, $C_6H_5 \cdot C \equiv C \cdot COOH$, by heating its cupric salt with water. In many respects it resembles acetylene, an example being the formation of metallic derivatives. Solution in concentrated sulphuric acid adds one molecule of water, forming acetophenone.

Alcohols and Aldehydes.

Cinnamyl alcohol, $C_6H_5 \cdot CH : CH \cdot CH_2OH$, is the only representative of the unsaturated alcohols requiring mention. It is a crystalline substance with an odour of hyacinths, and is present as an ester in storax. Careful oxidation converts it into cinnamic acid (**328**), and more vigorous oxidation into benzoic acid.

Cinnamaldehyde, $C_6H_5 \cdot CH{:}CH \cdot C\overset{H}{\underset{O}{}}$, is the chief constituent of oil of cinnamon, being obtainable from it through its sulphite compound. It is an oil of agreeable odour, and boils at 246°. It is resinified by strong acids, and with ammonia yields *hydrocinnamide*, $N_2(C_6H_5C_3H_3)_3$, analogous to hydrobenzamide (315).

Acids.

328. *Cinnamic acid*, $C_6H_5 \cdot CH{:}CH \cdot COOH$, is the most important unsaturated acid, and is present in certain balsams. Apart from resinous bodies, the main constituents of these substances are esters of cinnamic acid, benzoic acid, benzyl alcohol, and cinnamyl alcohol. Cinnamic acid is manufactured by a synthetic method discovered by SIR WILLIAM PERKIN. Benzaldehyde is heated with acetic anhydride, in presence of sodium acetate as a catalyst:

$$\underset{\text{Benzaldehyde}}{C_6H_5 \cdot C\overset{H}{\underset{O}{}}} + \underset{\text{Acetic anhydride}}{H_2CH \cdot CO \cdot O \cdot CO \cdot CH_3} = C_6H_5 \cdot CH{:}CH \cdot CO \cdot O \cdot CO \cdot CH_3 +$$

$$+ H_2O = \underset{\text{Cinnamic acid}}{C_6H_5 \cdot CH{:}CH \cdot COOH} + \underset{\text{Acetic acid}}{HO \cdot CO \cdot CH_3}.$$

PERKIN's synthesis can be effected with substituted benzaldehydes, as well as with homologues of acetic acid or with dibasic acids, it being possible by its aid to obtain a great number of unsaturated aromatic acids.

Cinnamic acid can be got also by the action of benzal chloride (321), $C_6H_5 \cdot CHCl_2$, on sodium acetate. It can be synthesized also by the condensation of malonic acid with benzaldehyde, a reaction induced readily by the catalytic influence of ammonia, one molecule of carbon dioxide being eliminated:

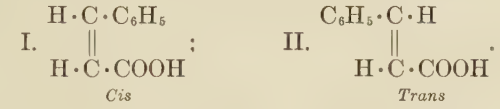
$$\underset{\text{Malonic acid}}{(HOOC)_2C\boxed{H_2+O}\overset{C \cdot C_6H_5}{\underset{H}{}}} = C_6H_5 \cdot CH{:}CH \cdot COOH + CO_2 + H_2O.$$

Cinnamic acid is a crystalline substance, melts at 134°, and dissolves with difficulty in cold water. In all respects it possesses the character of a substance with a double bond, and therefore forms addition-products and reduces VON BAEYER's reagent (113).

Its constitution indicates two stereoisomerides,

$$\begin{array}{l} C_6H_5\text{—}C\text{—}H \\ \qquad\quad \| \\ \quad H\text{—}C\text{—}COOH \end{array} \quad \text{and} \quad \begin{array}{l} C_6H_5\text{—}C\text{—}H \\ \qquad\quad \| \\ COOH\text{—}C\text{—}H \end{array},$$

to be possible, but four modifications are known. They are ordinary cinnamic acid, allo*cinnamic acid* melting at 68°, and two iso*cinnamic acids* melting at 58° and 42°. Biilmann proved the last three acids to be modifications of a single form, and therefore to afford an example of trimorphism. On inoculation with one of the forms, the liquid obtained by fusion of any of them crystallizes in that form. *Allo*cinnamic acid and the *iso*cinnamic acids can be prepared by partial reduction of phenylpropiolic acid, $C_6H_5 \cdot C{\equiv}C \cdot COOH$ (**327**), and therefore must have the *cis*-configuration (I), as is evident from a model. Consequently ordinary cinnamic acid has the *trans*-configuration (II):



It can be converted into the *cis*-form by exposing its solution in benzene to the ultraviolet rays of a "uviol" lamp for ten days.

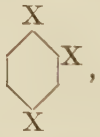
POLYSUBSTITUTED BENZENE DERIVATIVES.

329. A great number of polysubstituted derivatives of benzene is known, but only a few of special theoretical or technical interest will be considered. For the sake of systematic treatment, the substitution-products will be taken in the order adopted in the preceding pages for the monosubstituted derivatives. The polyhalogen compounds will be discussed first, then the substituted nitrobenzenes, sulphonic acids, phenols, and so on.

The general rule as to substituents simultaneously present exercising their normal functions holds, although the effect of a given substituent often is modified greatly by the presence of the other atoms or groups.

I. POLYHALOGEN DERIVATIVES.

The *polyhalogen derivatives* can be prepared by the direct action of chlorine or bromine on the aromatic hydrocarbons in presence of a catalyst, the anhydrous ferric halides being specially suitable for this purpose. The mode of procedure is to introduce a small proportion of dry iron-powder into the liquid, and pass in chlorine or add bromine drop by drop. If a halogen atom be attached already to the nucleus, replacement is mainly at the *para*-position, but the *ortho*-compound and a small proportion of the *meta*-compound are formed simultaneously. m-*Dichlorobenzene* and m-*dibromobenzene* can be prepared by reduction of *m*-dinitrobenzene (331), and subsequent diazotization of the product. The *para*-dihalogen compounds are solid, the isomeric *ortho*-compounds and *meta*-compounds are liquid. When three halogen atoms enter the nucleus, the main product is the 1:2:4-trihalogen-benzene,



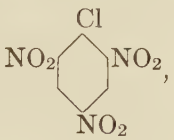
for each of the three dihalogen-benzenes yields the same derivative. Prolonged chlorination of benzene substitutes its six hydrogen atoms, with formation of Julin's *chlorocarbon*, C_6Cl_6, colourless needles melting at 229°. It is very stable, soluble with difficulty in most solvents, and is a product of the energetic chlorination of various benzene derivatives, the substituents already present being displaced by chlorine.

II. HALOGEN-NITRO-COMPOUNDS.

330. Nitration of a monohalogen-benzene yields only the *ortho*-compound and the *para*-compound, the second being formed in larger proportion. An example is furnished by the nitration of monochlorobenzene, at the ordinary temperature the product consisting of about 70 per cent. of p-*chloronitrobenzene*, and about 30 per cent. of of o-*chloronitrobenzene*, $Cl \cdot C_6H_4 \cdot NO_2$. m-*Chloronitrobenzene* is prepared readily by chlorination at elevated temperature of a mixture of nitrobenzene with 20 per cent. of its weight of antimony pentachloride. *m*-Halogen-nitrobenzenes can be prepared also from *m*-nitroaniline by the diazotization-method.

Unlike the halogen in the monohalogen-benzenes, that in the *p*-halogen-nitrobenzenes and the *o*-halogen-nitrobenzenes is characterized by its power of taking part in double decompositions. When these substances are heated with an alcoholic solution of sodium methoxide, the halogen atom is replaced by the methoxyl-group; with alcoholic ammonia the halogen atom is exchanged for the amino-group. A contrast is presented by the *m*-halogen-nitrobenzenes, their halogen being almost as difficult to replace as that in the unsubstituted monohalogen-benzenes.

The presence of several nitro-groups in the nucleus at the *ortho*-position and the *para*-position to halogen causes a marked increase in the adaptability for double decomposition. The chlorine atom in *picryl chloride*,



is replaceable by a great variety of substituents. This substance has the character of an acid chloride, being converted by hot water into hydrogen chloride and picric acid, $C_6H_2(NO_2)_3OH$, and by ammonia into picramide, $C_6H_2{}^{(NO_2)_3\ 2:4:6}_{NH_2\ 1}$.

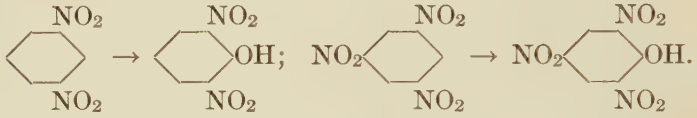
III. POLYNITRO-DERIVATIVES.

331. m-*Dinitrobenzene* is obtained by the nitration of benzene with a mixture of concentrated sulphuric acid and fuming nitric acid. It forms colourless needles melting at 90°. As its reduction yields m-*phenylenediamine*, it is employed in the preparation of coal-tar dyestuffs. It is utilized also in the manufacture of explosives, for it can be exploded by mercury fulminate. In addition to the *m*-compound, a small proportion of o-*dinitrobenzene* and traces of p-*dinitrobenzene* are formed. Stronger nitration, effected by a mixture of nitric acid

and fuming sulphuric acid at 140°, converts *m*-dinitrobenzene into *symmetrical trinitrobenzene* (1:3:5), melting at 121°.

Symmetrical trinitrotoluene, known as "TNT," is manufactured by the nitration of toluene in successive stages. It is one of the most powerful explosives known, especially when mixed with ammonium nitrate, and was employed extensively in the great European war of 1914–1918.

The hydrogen atoms and nitro-groups in the polynitrobenzenes are replaced much more readily than those in mononitrobenzene. Examples are the conversion of *m*-dinitrobenzene by oxidation into 2: 6-*dinitrophenol*, and of 1:3:5-trinitrobenzene into 2:4:6-trinitrophenol, or *picric acid*:

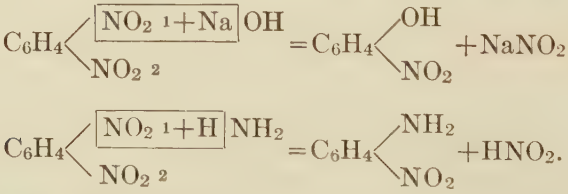


By the action of sodium ethoxide or methoxide, one of the nitro-groups in *o*-dinitrobenzene or *p*-dinitrobenzene can be replaced by ethoxyl or methoxyl:

$$C_6H_4{<}\begin{matrix}NO_2\\NO_2\end{matrix}+NaOCH_3=C_6H_4{<}\begin{matrix}OCH_3\\NO_2\end{matrix}+NaNO_2.$$

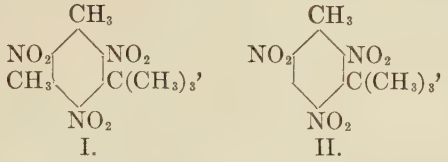
A remarkable phenomenon is the inability of *m*-dinitrobenzene to undergo this substitution, although in 1:3:5-trinitrobenzene, with each of its substituents in the *meta*-position to the other two, one of the nitro-groups can be replaced readily by methoxyl ("Laboratory Manual," XXXIII, 3).

Boiling with sodium hydroxide converts *o*-dinitrobenzene into o-*nitrophenol*, and heating with alcoholic ammonia gives o-*nitroaniline*:



It has not been possible to introduce more than three nitro-groups into benzene by direct nitration, substitution even by the third nitro-group meeting with considerable opposition. The homologues of benzene are converted into their higher nitro-derivatives much more readily than benzene itself.

Trinitrobutyl-m-*xylene* (I) and *trinitro*-m-*butyltoluene* (II),



I. II.

are employed in the perfume industry on account of their powerful, musk-like odour, the first being the technical product termed "Artificial musk." This property is associated partly with the presence of the trimethyl-methyl-group, and partly with the fact of this group occupying the *meta*-position with respect to a methyl-group. The isomeride with these groups at the *para*-position is odourless. Natural musk derived from the male musk-deer owes its odour to the presence of muscone (**277**), a substance without any analogy in composition to artificial musk. It is therefore possible for substances of wholly different constitution to have the same odour.

IV. SUBSTITUTED BENZENESULPHONIC ACIDS.

332. Digestion of monochlorobenzene or monobromobenzene with concentrated sulphuric acid, or better with the fuming acid, yields exclusively p-*chlorobenzenesulphonic acid* or p-*bromobenzenesulphonic acid*. The properties of these substances approximate closely to those of the unsubstituted benzenesulphonic acid.

Fusion with potassium hydroxide converts each of the three bromobenzenesulphonic acids into resorcinol, $C_6H_4{<}^{OH^1}_{OH^3}$, one of the few instances of substitution at a position other than that occupied by the group replaced. Additional examples of the same phenomenon are mentioned subsequently (**333**).

Both nitration of benzenesulphonic acid and sulphonation of nitrobenzene yield chiefly m-*nitrobenzenesulphonic acid*, with simultaneous production of a small percentage of the isomeric ortho-*compound* and para-*compound*.

Heating benzene and its homologues at a high temperature with fuming sulphuric acid produces *disulphonic acids* and *trisulphonic acids*, but it has not been found possible to introduce more than three sulpho-groups. Addition of silver sulphate greatly facilitates the formation of *benzenetrisulphonic acid*. With respect to the production of disulphonic acids, benzene yields chiefly *benzene*-m-*disulphonic acid*, a substance converted partially into *benzene*-p-*disulphonic acid* by prolonged heating at a high temperature with sulphuric acid. Inversely, under the same conditions the *para*-compound is transformed partially into *benzene*-m-*disulphonic acid*. *Benzene*-o-*disulphonic acid* is not produced by direct sulphonation of benzene.

V. SUBSTITUTED PHENOLS AND POLYHYDRIC PHENOLS.

Halogen-phenols.

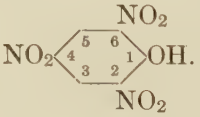
333. The direct action of chlorine or bromine on phenol yields o-*chlorophenol* and p-*chlorophenol*, or o-*bromophenol* and p-*bromophenol*. These compounds are formed also by reduction of the halogen-nitrobenzenes, with subsequent diazotization of the products. In aqueous solution the halogenation is not limited to the entrance of one halogen atom, but yields higher products, an example being the precipitation of 2:4:6-tribromophenol by addition of bromine-water at the ordinary temperature to an aqueous solution of phenol (293). The *ortho*-compounds have a pungent and very penetrating odour. At the ordinary temperature, the *ortho*-isomerides and the *meta*-isomerides of the chlorophenols and the bromophenols are liquid, the *para*-isomerides being solid (285). Fusion with potassium hydroxide replaces their halogen by hydroxyl, although the corresponding hydroxy-derivative is not always formed (332). The acidic character of the phenols is strengthened considerably by the introduction of halogen, exemplified by the power of trichlorophenol to decompose carbonates.

Iodine can substitute hydrogen in phenol only in presence of an oxidizer, the hydrogen iodide being prevented by oxidation from eliminating the iodine atom from the iodophenol.

Nitrophenols.

The increased aptitude for substitution displayed by the hydrogen atoms of the benzene-nucleus after introduction of a hydroxyl-group is illustrated by the behaviour of the phenols towards nitric acid. To obtain nitrobenzene from benzene, it is necessary to employ concentrated nitric acid, but phenol is converted by dilute nitric acid at low temperatures into o-*nitrophenol* and p-*nitrophenol*. The two isomerides can be separated by distillation with steam, only the *ortho*-compound being volatile. m-*Nitrophenol* can be prepared from *m*-nitroaniline by the diazo-reaction. *o*-Nitrophenol has a yellow colour and a characteristic odour. *m*-Nitrophenol and *p*-nitrophenol are colourless, but resemble the *ortho*-compound in forming highly coloured phenoxides. Further particulars of the nitrophenols are given in 330 and 331.

334. The most important nitrophenol derivative is *picric acid*, or 1:2:4:6-*trinitrophenol*,



This substance has been known for a long time, and is produced by the action of concentrated nitric acid on many substances, such as silk, leather, resins, aniline, and indigo. It is prepared by dissolving phenol in concentrated sulphuric acid, and carefully adding small quantities of this solution to concentrated nitric acid of density 1·4. It can be obtained also directly from benzene by heating with nitric acid and mercuric nitrate. Under the influence of this salt, phenol is formed by the action of the nitric acid on the hydrocarbon, and is nitrated immediately. Picric acid is not susceptible to further nitration, being the final product of the action of nitric acid on phenol. This fact explains its production by the action of nitric acid on such heterogeneous substances.

Pure solid picric acid has only a very faint yellow colour, but its aqueous solution is deep yellow. It is a strong acid, undergoing considerable ionization by solution in water. The yellow colour is characteristic of the anion, for the unionized solution of this acid in light petroleum is colourless. The anion also undergoes tautomerization. The acid is slightly soluble in cold water, and is not volatile with steam. It melts at 122°, and its excessively bitter taste suggested its name (πικρός, bitter).

A consideration of the following reactions shows picric acid to be comparable with the carboxylic acids. Phosphorus pentachloride replaces the hydroxyl-group by chlorine, with formation of *picryl chloride* (330). Silver picrate and methyl iodide yield *methyl picrate*, a substance with the properties of an ester, being saponified by boiling with concentrated caustic alkalis, and with ammonia yielding picramide. These facts afford further evidence of the remarkable increase in the reactivity of the hydroxyl-group, due to the presence of the three nitro-groups.

Picric acid yields well-defined crystalline, explosive salts of a yellow or red colour. The potassium salt dissolves with difficulty in water, and resembles the ammonium salt in being exploded by percussion, although the acid itself is not. Prolonged consumption of small quantities of potassium picrate imparts a yellow colour first to the *conjunctiva* of the eyes, and later to the entire skin.

The acid yields molecular compounds with many aromatic hydrocarbons, that with naphthalene having the formula $C_{10}H_8 \cdot C_6H_2(NO_2)_3 \cdot OH$, and melting at 149°. These derivatives crystallize well, and have definite melting-points. Sometimes they are employed with advantage in the separation of hydrocarbons, or in their identification. Picric acid is eliminated from them by the action of ammonia.

The acid can be detected by an aqueous solution of potassium

cyanide, a red coloration due to the formation of *iso*purpuric acid being developed by addition of that reagent.

Picric acid is employed as an explosive not leaving any residue on explosion, and termed " lyddite." Formerly it was utilized as a dyestuff, imparting a yellow colour to wool and to silk.

Phenolsulphonic Acids.

o-*Phenolsulphonic acid* and p-*phenolsulphonic acid* are obtained by dissolving phenol in concentrated sulphuric acid. m-*Phenolsulphonic acid* is produced by fusing *m*-benzenedisulphonic acid with potassium hydroxide. The *ortho*-acid is characterized by its easy conversion into the *para*-compound. Phenol sulphonates more readily than benzene, its solution in sulphuric acid being transformed into the *o*-sulphonic acid and *p*-sulphonic acid even at the ordinary temperature.

Nitrosophenol.

335. In certain respects *nitrosophenol* reacts in accordance with the constitution $C_6H_4{<}^{NO}_{OH}$, although its formation from quinone and hydroxylamine points to the structure $C_6H_4{<}^{NOH}_{O}$. It is prepared by the action of nitrous acid on phenol, or of potassium hydroxide on nitrosodimethylaniline (**299**):

$$C_6H_4{<}^{\boxed{H+HO}\,NO}_{OH} = C_6H_4{<}^{NO}_{OH} + H_2O;$$

$$ON\text{-}C_6H_4\text{-}\underline{\boxed{N(CH_3)_2+H}}\,OH = HN(CH_3)_2 + ON\text{-}C_6H_4\text{-}OH.$$

Like other oximes, nitrosophenol, or quinone mono-oxime, unites with bases. It is a colourless compound, crystallizing in needles soon turned brown by exposure to air. In oxidation and reduction it behaves as nitrosophenol, yielding nitrophenol by the first process, and aminophenol by the second.

336. Phenol is attacked by oxidizers much more readily than benzene (**293**). The *polyhydric phenols* possess this property to an even greater extent, the alkali solutions of many of them behaving as powerful reducers.

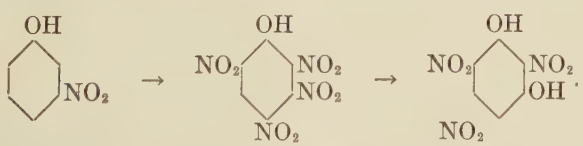
Dihydric Phenols.

The *o*-compound, $C_6H_4<^{OH\ 1}_{OH\ 2}$, *catechol* (" pyrocatechol " or " pyrocatechin "), is a constituent of many resins, and can be prepared by fusing *o*-phenolsulphonic acid with potassium hydroxide.

Catechol is crystalline and readily soluble in water, alcohol, and ether. It melts at 104°. Its alkaline solution is turned green by atmospheric oxidation, and then becomes black. Its aqueous solution precipitates metallic silver from silver-nitrate solution at the ordinary temperature, and gives a green coloration with ferric chloride. The monomethyl ether, $C_6H_4<^{OCH_3\ 1}_{OH\ 2}$, is termed *guaiacol*, and is present in the tar obtained by the dry distillation of beechwood. Heating with hydrogen iodide converts guaiacol into catechol and methyl iodide. The dimethyl ether of catechol is named *veratrole*, and is characterized by its agreeable odour.

Resorcinol (" resorcin "), or *m*-dihydroxybenzene, $C_6H_4<^{OH\ 1}_{OH\ 3}$, can be obtained by fusing *m*-phenylenedisulphonic acid, $C_6H_4<^{SO_3H\ 1}_{SO_3H\ 3}$, with potassium hydroxide, the method for its manufacture. It yields a deep-violet coloration with ferric chloride, and bromine-water converts it into 2:4:6-*tribromoresorcinol*. It is a colourless crystalline substance melting at 118°, and is readily soluble in water, alcohol, and ether. It quickly turns brown owing to the action of the air. A delicate test for resorcinol is mentioned in 348.

Styphnic acid, $C_6H^{(OH)_2(1:3)}_{(NO_2)_3(2:4:6)}$ is a type of a nitrated dihydroxybenzene, and is obtained by the action of cold nitric acid on resorcinol, as well as from certain gum-resins by the same means. The conversion of *m*-nitrophenol into styphnic acid by the agency of nitric acid involves the intermediate formation of a tetranitro-compound with one of its nitro-groups so reactive as to be replaceable by hydroxyl through the action of water, styphnic acid being formed:



m-Nitrophenol — 2:3:4:6-Tetranitrophenol — Styphnic acid

Quinol (" hydroquinone "), or *p*-dihydroxybenzene, melts at 170°. Its chief characteristic is the loss by oxidation of two hydrogen atoms

with formation of *quinone*, $C_6H_4O_2$ (338) a substance reconverted into quinol readily by reduction. The reducing effect of quinol is employed in photography for the development of negatives and prints. With ammonia it gives a red-brown coloration, due to the formation of complex derivatives. Like its isomerides, it is readily soluble in water.

The dihydroxybenzenes can be separated by the action of lead acetate. With this reagent, catechol gives a white precipitate, resorcinol does not yield a precipitate, and quinol gives a precipitate only in presence of ammonia.

Litmus is a derivative of *orcinol* or symmetrical dihydroxytoluene,

$$C_6H_3\begin{cases}CH_3\ 1\\OH\ 3\\OH\ 5\end{cases}.$$

Trihydric Phenols.

337. *Pyrogallol* ("pyrogallic acid"), $C_6H_3\begin{cases}OH\ 1\\OH\ 2\\OH\ 3\end{cases}$, is obtained by heating *gallic acid* (345), carbon dioxide being eliminated:

$$\underset{\text{Gallic acid}}{C_6H_2(OH)_3\cdot COOH} = \underset{\text{Pyrogallol}}{C_6H_3(OH)_3} + CO_2.$$

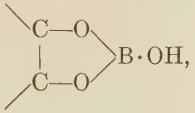
Pyrogallol forms crystals melting at 132°, and is soluble readily in water. In alkaline solution it is a strong reducer, rapidly absorbing the oxygen of the atmosphere, with formation of a brown coloration. For this reason it is employed in gas-analysis to remove oxygen from mixtures. It also finds application as a developer in photography, and as an agent for dyeing furs.

Mention has been made of the influence exerted by boric acid on the conductivity of hydroxy-derivatives (231). The results obtained by Böeseken in his investigation of the effect of this acid on the polyhydric phenols possess a general significance. Of the three dihydroxybenzenes, catechol alone has its electric conductivity in aqueous solution greatly augmented by the addition of boric acid. With pyrogallol the effect is similar, but not with the other polyhydric phenols. A seminormal solution of boric acid was found to have a conductivity of $25{\cdot}7\times10^{-6}$, that of a similar solution of catechol being $13{\cdot}6\times10^{-6}$. A solution containing both substances in seminormal concentration had the conductivity $555{\cdot}2\times10^{-6}$, the sum of the conductivity values for boric acid and catechol separately being only $(25{\cdot}7+13{\cdot}6)\times10^{-6}=39{\cdot}3\times10^{-6}$.

The conductivity of a seminormal solution of resorcinol was found to be $5{\cdot}7\times10^{-6}$, and that of an equivalent solution of boric acid and resorcinol to be $25{\cdot}0\times10^{-6}$ instead of $(25{\cdot}7+5{\cdot}7)\times10^{-6}=31{\cdot}4\times10^{-6}$. For catechol there is an enormous increase in conductivity, but for resorcinol a slight diminution.

Both catechol and pyrogallol have two hydroxyl-groups in union with

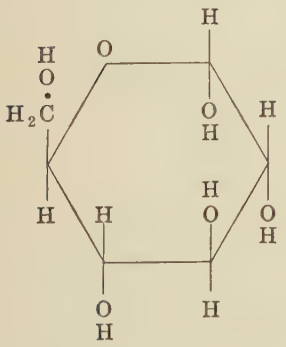
two carbon atoms directly attached, but this fact does not explain the increase of conductivity, for glycol, $CH_2OH \cdot CH_2OH$, lacks the characteristic. An explanation is furnished by assuming the hydroxyl-groups of these two phenols to be situated in the same plane as the carbon atoms, so as to make possible the formation of a ring-system of the type



with a degree of dissociation much higher than boric acid alone.

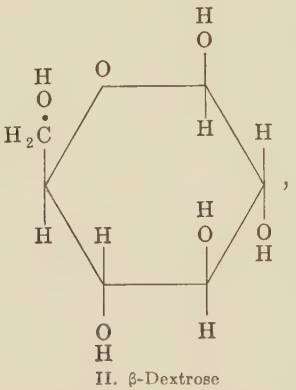
The influence exerted by boric acid on the conductivity of polyhydric alcohols in aqueous solution obviously affords an aid in the determination of the configuration of these substances. Applied to glycol, this method indicates the two hydroxyl-groups not to be in corresponding positions, but as in the configuration $\begin{matrix} HO \cdot CH_2 \\ | \\ H_2C \cdot OH \end{matrix}$. The conductivity of boric acid is raised by glycerol, erythritol, mannitol, dulcitol, and sorbitol, indicating the presence in each of these substances of at least two hydroxyl-groups in corresponding positions.

Böeseken discovered a very important relationship between the influence of boric acid on the conductivity of α-dextrose and β-dextrose and the phenomenon of mutarotation (**208**). This property of mutarotation is explained by assuming the partial conversion of the two forms α and β into one another until equilibrium is attained. Investigation of the stereochemical constitutions of α-dextrose and β-dextrose (**220**) indicates the two possible configurations to be



I. α-Dextrose

and



II. β-Dextrose

the hexagon in each formula representing the plane of the ring of five carbon atoms and one oxygen atom contained in dextrose. Prior to Böeseken's work there was no evidence available as to the particular formula representing the α-modification, or as to that corresponding with

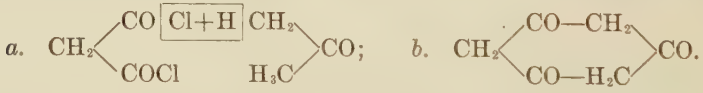
the β-form. In formula I there are two hydroxyl-groups on the same side of the plane of the ring, but not in formula II. A substance with the first formula should show a greater increase in conductivity on addition of boric acid than one with the second formula. As a result of the approach to equilibrium between I and II, the increased conductivity of I must diminish slowly, the change being accompanied by a gradual rise in the conductivity of II. This phenomenon is analogous to the diminution with lapse of time of the optical rotation produced by one modification and the corresponding rise in rotatory power of the other isomeride.

Experiment has proved boric acid+α-dextrose to have diminishing conductivity, and has demonstrated an increasing conductivity for boric acid +β-dextrose. Formula I accordingly is assigned to α-dextrose, and formula II to β-dextrose.

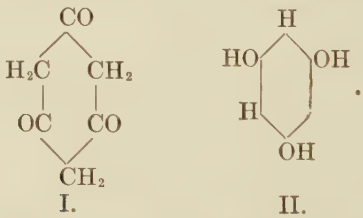
The results of later research confirmed this view, elimination of one molecule of water from α-dextrose yielding the anhydride, *glucosan*. The presence of the two hydroxyl-groups on the same side of the plane of the ring affords an excellent explanation of the formation of this anhydride (**220**).

Phloroglucinol, (symmetrical trihydroxybenzene), $C_6H_3\langle{}^{OH\ 1}_{OH\ 2}_{OH\ 3}$, is formed by fusing various resins with potassium hydroxide. It is crystalline, and gives a deep-violet coloration with ferric chloride. A remarkable synthesis of phloroglucinol is described in the next paragraph.

On heating in presence of calcium carbonate to neutralize the hydrogen chloride formed, malonyl chloride and acetone in equivalent proportions react to give the condensation-product *a*, convertible almost quantitatively into phloroglucinol (*b*) by further heating with water and calcium carbonate:



Phloroglucinol should therefore have constitution I:



I. II.

It is *cyclo*hexane with three of the methylene-groups, CH_2, replaced by carbonyl, CO, and must therefore be termed *triketo*cyclo*hexane*. The behaviour of phloroglucinol has been found to accord with this constitution, for with three molecules of hydroxylamine it yields a trioxime. Phloroglucinol has also the character of a phenol, yielding with acetyl chloride a triacetate.

It exists, therefore in two tautomeric forms, as a hexamethylene derivative, I, and as trihydroxybenzene, II.

This phenomenon is a remarkable example of the alteration of the positions of the atoms (the hydrogen of the hydroxyl-groups) in the molecule, resulting in the conversion of a benzene derivative into a derivative of hexamethylene.

This view explains the interaction of phloroglucinol, and other polyhydric phenols, and a mixture of potassium hydroxide and an alkyl iodide to form derivatives with alkyl-groups attached to carbon and not to oxygen; for the hydrogen in the methylene-groups of the tautomeric form must be replaceable by metals (200).

The problem of assigning the enolic or ketonic formula to free phloroglucinol has been solved by the aid of a method of valuable service in many other examples of analogous nature. The process was discovered by Hartley, and involves the study of the absorption-spectra in the ultraviolet region of the spectrum.

An electric arc between iron electrodes is arranged, the light from this source being very rich in bands in the ultraviolet region. After resolution by means of a quartz prism, the beam is passed through an aqueous or alcoholic solution of known strength of the substance under examination. The absorption-band or absorption-bands can be photographed. They are caused by the presence of the dissolved substance, because they are not produced by water or alcohol alone. By this method the absorption-bands for a number of solutions of increasing dilution, or better for a number of liquid layers of diminishing thickness, are reproduced, and the process is continued until the absorption-bands vanish owing to the dilution being too great, or the thickness of the layer being too small.

The photographs obtained are placed so as to bring the wave-lengths λ or the oscillation-frequencies $\frac{1}{\lambda}$ (the abscissæ) together. On drawing a line through the edges of the various absorption-bands, a curve like that depicted in Fig. 74 is produced. To reduce the length of the figure, it is constructed by employing the logarithms of the layer-thicknesses as ordinates instead of these thicknesses themselves. The figure indicates the substance under examination to have two absorption-bands, at *ABC* and *DEF*. The second band is much more persistent than the first, and therefore does not vanish until the layer has become correspondingly thinner.

From numerous measurements by this method, Hartley established a general rule as to the inability of aliphatic compounds, and the capacity of aromatic derivatives, to give absorption-bands, and

demonstrated the absorption-bands produced by aromatic tautomerides to exhibit sometimes marked differences in position and persistence. The method affords an excellent aid in the detection of obscure examples of isomerism indistinguishable by chemical tests only.

Application of HARTLEY's method to phloroglucinol revealed it and its trimethyl ether to give nearly the same absorption-band. The ether being converted into phloroglucinol by heating with hydrochloric acid, its methyl-groups must be in union with oxygen. The absorption-

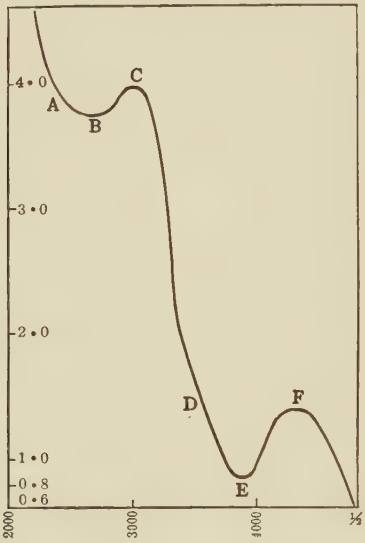


FIG. 74.—HARTLEY'S ABSORPTION-CURVE.

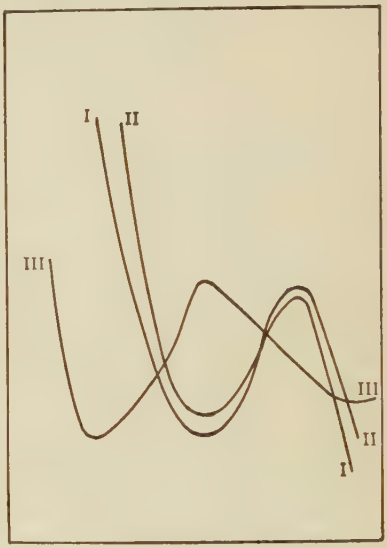
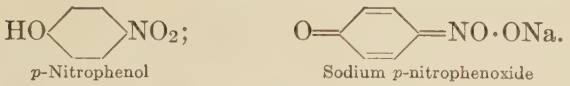


FIG. 75.—ABSORPTION-CURVES OF *p*-NITROPHENOL, *p*-NITROANISOLE, AND SODIUM *p*-NITROPHENOXIDE.

band also occupies almost the same position as that of pyrogallol, a substance devoid of tautomerism. On the analogy of *cyclo*hexadione, the tautomeric form of phloroglucinol or *cyclo*hexatrione should not give an absorption-band. It is therefore logical to assign the enolic formula to free phloroglucinol.

This method also furnished valuable evidence of a difference in constitution between free nitrophenol and its deeply-coloured salts. Fig. 75 represents the absorption-curve of a neutral solution of *p*-nitrophenol (I), that of a solution of the methyl ether *p*-nitroanisole (II), and that of a solution of sodium *p*-nitrophenoxide (III). Curves I and II almost coincide, and the difference in character of curve III is explained by assuming a *quinonoid* structure (373) for the nitrophenoxide:



p-Nitrophenol Sodium *p*-nitrophenoxide

Similar differences observed between the esters and the salts of the ordinary acids containing a carboxyl-group indicate the constitution of the salts to be quite different from that of the esters.

Higher Phenols.

The chief of the *higher phenols* is *hexahydroxybenzene*, $C_6(OH)_6$. Its potassium derivative, *potassium carbonyl*, $C_6(OK)_6$, is formed in the preparation of potassium, and acquires an explosive character through exposure to air ("Inorganic Chemistry," **229**). It can be obtained by heating potassium in a current of carbon monoxide, a direct synthesis of a derivative of benzene. Distillation with zinc-dust converts hexahydroxybenzene into benzene. It is a white crystalline substance, and undergoes oxidation very readily.

Quinones.

338. The *quinones* are substances derived by the elimination of two hydroxyl-hydrogen atoms from aromatic dihydroxy-derivatives:

$$\underset{\text{Dihydroxybenzene}}{C_6H_4(OH)_2} - 2H = \underset{\text{Quinone}}{C_6H_4O_2}.$$

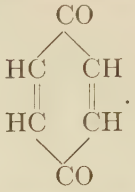
The simplest quinone is *benzoquinone*, $C_6H_4O_2$, a substance also termed *quinone*. It is obtained by the oxidation of many *para*-derivatives of benzene, such as *p*-aminophenol $C_6H_4 < \overset{NH_2\ 1}{OH\ 4}$, sulphanilic acid, $C_6H_4 < \overset{NH_2\ 1}{SO_3H\ 4}$, and *p*-phenolsulphonic acid, $C_6H_4 < \overset{OH\ 1}{SO_3H\ 4}$, and also by the oxidation of aniline with chromic acid, the ordinary method for its preparation. In this reaction the aniline can be assumed to undergo a preliminary transformation into phenylhydroxylamine, $C_6H_5 \cdot NHOH$, this substance then changing to *p*-aminophenol, $HO \cdot C_6H_4 \cdot NH_2$ (**303**). Benzoquinone is formed also in the oxidation of quinol (**336**), though that substance is prepared usually by the reduction of quinone. Oxidation of quinol by ferric chloride yields *quinhydrone*, a compound in equimolecular proportions of quinone and quinol, crystallizing in beautiful, intensely coloured, long needles.

o-Dihydroxybenzene or catechol also can be converted into an unstable quinone by the action of silver oxide. *m*-Dihydroxybenzene or resorcinol does not yield a quinone.

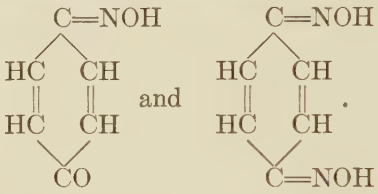
A great number of *para*-quinones is known. Like benzoquinone, they can be prepared by oxidizing the corresponding *para*-compounds.

The quinones are yellow, and have a peculiar pungent odour. They

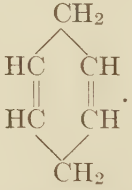
volatilize with steam with partial decomposition, and have oxidizing properties. The constitution of benzoquinone is expressed best by



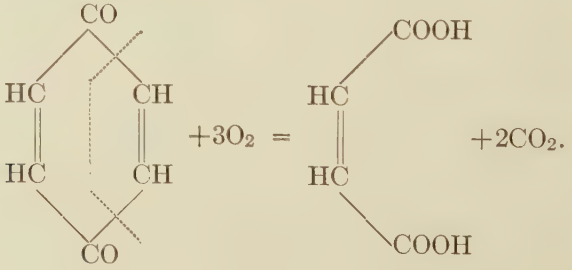
Such a formula requires benzoquinone to be a diketone, and to contain two double bonds, and in its properties it fulfils both conditions. Its ketonic character is inferred from its yielding with hydroxylamine first a *quinone mono-oxime* (335), and then a *quinone dioxime*:



The presence of double bonds is indicated by its power of forming addition-products, benzoquinone in chloroform solution being able to add four atoms of bromine. According to this constitution, benzoquinone is not a true benzene derivative, but the diketone of a *p*-dihydrobenzene:



This formula is supported by the oxidation of benzoquinone to maleic acid, effected by an alkali-metal persulphate in presence of silver sulphate and sulphuric acid:



VI. SUBSTITUTION-PRODUCTS OF ANILINE.

339. Aniline is attacked very energetically by chlorine and bromine. The direct introduction of these halogens must be effected by their slow addition to a solution of acetoanilide in glacial acetic acid, the main products being the *para*-compounds. The *ortho*-halogen-anilines and the *meta*-halogen-anilines are prepared by reduction of the corresponding halogen-nitrobenzenes. The production of 2:4:6-*tribromoaniline* is described in **296**. The basic character of aniline is weakened by the introduction of halogens.

Nitroanilines.

Nitroanilines are compounds containing nitro-groups and an amino-group, and can be obtained by the partial reduction of dinitro-compounds by means of ammonium sulphide. Another method for their production consists in the nitration of anilines, though the direct action of nitric acid on those bases yields mainly oxidation-products. For nitration, the amino-group must be "protected" against the action of this acid, either by preliminary conversion of the aniline into acetoanilide, or by causing the nitric acid to react in presence of a large proportion of sulphuric acid. With the acetyl-compound, p-*nitroaniline* is the chief product; with sulphuric acid, m-*nitroaniline* and *p*-nitroaniline are formed in almost equal ratio, and a very small proportion of o-*nitroaniline*.

The nitroanilines can be prepared also from the corresponding chloronitrobenzenes and bromonitrobenzenes (**330**). There is a marked weakening of the basic character in these substances, most pronounced in the *ortho*-derivatives, and least in the *meta*-compounds.

> Addition of a large excess of water to a solution of *o*-nitroaniline in concentrated sulphuric acid precipitates yellow *o*-nitroaniline owing to almost complete hydrolysis of the salt. With *p*-nitroaniline there is no precipitation, but the solution develops a yellow colour, the hydrolysis being very much less. A similar operation with *m*-nitroaniline yields a colourless solution, the salt not being hydrolyzed.

o-Nitroaniline, *m*-nitroaniline, and *p*-nitroaniline, $C_6H_4{<}^{NO_2}_{NH_2}$, are yellow crystalline compounds, almost insoluble in cold water, but soluble readily in alcohol. Their melting-points in the order given are 71°, 114°, and 147°.

The amino-groups in *o*-nitroaniline and *p*-nitroaniline, but not that in *m*-nitroaniline, are exchanged for hydroxyl by heating with a solu-

tion of potassium hydroxide, the corresponding potassium nitrophenoxide being formed. The amino-group in *picramide* or 2 : 4 : 6-*trinitroaniline*, $C_6H_2(NO_2)_3 \cdot NH_2$, is replaced very readily by hydroxyl.

p-Aminobenzenesulphonic Acid or Sulphanilic Acid.

Sulphanilic acid is obtained by heating aniline sulphate or by heating *p*-chlorobenzenesulphonic acid at 200° with ammonia in presence of copper as a catalyst. Like its isomerides, it dissolves with difficulty in cold water. The basic properties of aniline are weakened greatly by the introduction of the sulpho-group into the ring, for sulphanilic acid cannot yield salts with acids, whereas the sulpho-group reacts with bases to form salts. The formula of sulphanilic acid is probably that of an inner salt, $C_6H_4<\begin{matrix}SO_3\\NH_3\end{matrix}>$. Its fusion with potassium hydroxide does not yield aminophenol in accordance with precedent, but aniline. Oxidation with chromic acid converts it into benzoquinone. Dilute sulphuric acid precipitates from the aqueous solution of a mixture of sodium sulphanilate and sodium nitrite an inner salt of *benzenediazoniumsulphonic acid*, a substance nearly insoluble in water:

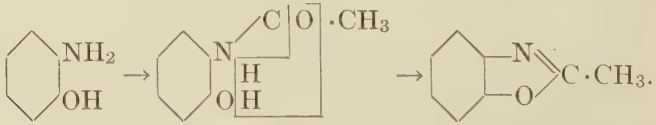
$$C_6H_4<\begin{matrix}N_2\cdot\\SO_3\end{matrix}\Big|\begin{matrix}OH\\H\end{matrix}=H_2O+C_6H_4<\begin{matrix}N_2\\SO_3\end{matrix}>.$$

This compound is of great importance in the preparation of azo-dyestuffs, such as *helianthine* (341).

Aminophenols.

Aminophenols are formed by the reduction of nitrophenols. The acidic character in these compounds is so weakened as to render them unable to combine with bases, but they yield salts with acids. In the free state the aminophenols are colourless solids crystallizing in leaflets, and readily turned brown by atmospheric oxidation with formation of a resin. Their hydrochlorides are more stable.

o-*Aminophenol* yields compounds by the substitution of acid-residues in the amino-group, water being eliminated instantaneously, and *anhydro-bases* formed:



Acetyl-derivative — Ethenylaminophenol, Anhydro-base

Acids regenerate aminophenol and acetic acid.

p-*Aminophenol* is obtained by the electro-reduction of nitrobenzene in acid solution (303).

Unless sodium sulphite be present, the alkaline solution of *p*-aminophenol rapidly acquires a dark colour. The trade-name of the solution containing that sulphite is "Rodinal." It finds application as a photographic developer.

Lumière discovered certain general conditions determining the applicability of aromatic compounds to photographic development. They must contain either some hydroxyl-groups or some amino-groups, or at least one of each class. To obviate interference with development by the presence of substituents in the amino-group and in the hydroxyl-group, the molecule must contain not less than two such unsubstituted groups.

A derivative of *p*-aminophenol employed in medicine is "Phenacetin" or *acetylphenetidine*, $C_6H_4<\begin{matrix}OC_2H_5\\NH\cdot C_2H_3O\end{matrix}$, the acetamino-derivative of phenetole, $C_6H_5\cdot OC_2H_5$.

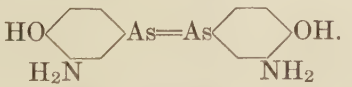
Heating aniline hydroarsenate, $C_6H_5\cdot NH_2,H_3AsO_4$, eliminates a molecule of water, and forms p-*aminophenylarsinic acid*, $NH_2\cdot C_6H_4\cdot AsO(OH)_2$. The presence of a free amino-group is indicated by the possibility of diazotizing the compound. Iodine converts it into *p*-iodoaniline, with elimination of the arsinic-acid residue. The formation of *p*-aminophenylarsinic acid is analogous to that of sulphanilic acid by heating aniline hydrogen sulphate:

$$\underset{\text{Aniline hydrogen sulphate}}{C_6H_5\cdot NH_2,H_2SO_4}-H_2O=\underset{\text{Sulphanilic acid}}{NH_2\cdot C_6H_4\cdot SO_3H}.$$

Sodium p-*aminophenylarsinate* or "Atoxyl," and *sodium* p-*acetylaminophenylarsinate* or "Arsacetin," $CH_3\cdot CO\cdot NH\cdot C_6H_4\cdot AsO<\begin{matrix}OH\\ONa\end{matrix}$, are valuable remedies for the treatment of *trypanosomiasis* or sleeping sickness.

Heating phenol with arsenic acid yields the analogous p-*hydroxyphenylarsinic acid*, $HO\cdot C_6H_4\cdot AsO(OH)_2$, converted by careful nitration into 3-*nitro*-4-*hydroxyphenylarsinic acid*,

Reduction transforms this product into the corresponding *diaminodihydroxyarsenobenzene*,



The *dihydrochloride* of this substance is the "Salvarsan" discovered by Ehrlich and Hata, and has been employed with good results in the treatment of diseases of protozoal origin. It is a crystalline powder readily soluble in hot water, but the solution decomposes rapidly.

With silver nitrate it yields a complex *silver-salvarsan*, characterized by even greater therapeutic efficacy.

Polyamino-compounds are obtained by the reduction of polynitro-derivatives. m-*Phenylenediamine*, $C_6H_4{<}^{NH_2\ 1}_{NH_2\ 3}$, is formed from benzene by nitration and subsequent reduction.

p-*Phenylenediamine* can be prepared by the reduction of amino-azobenzene (**309**) with tin and hydrochloric acid, aniline also being formed:

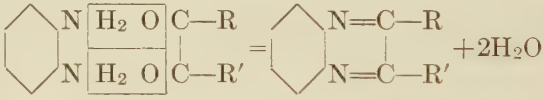
$$C_6H_5\cdot N{:}\,{}^{1}N\cdot C_6H_4\cdot {}^{4}NH_2 + 2H + 2H = C_6H_5\cdot NH_2 + H_2{}^{1}N\cdot C_6H_4\cdot {}^{4}NH_2.$$

Triaminobenzenes are prepared similarly (**341**).

At temperatures between 180° and 200° with cupric sulphate as a catalyst, *p*-dichlorobenzene and *p*-chloroaniline are converted by aqueous ammonia into the corresponding diamine.

Most of the polyaminobenzenes are crystalline solids, and distil without decomposition. They dissolve readily in warm water.

The three diaminobenzenes are distinguished by the following series of reactions. The *o*-diamines react readily with 1:2 diketones, yielding *quinoxalines*:



m-Phenylenediamine in aqueous solution gives an intense brown coloration with nitrous acid, even when the acid solution is very dilute (**341**). *p*-Phenylenediamine is converted by oxidation into benzoquinone.

Like the polyhydric phenols, the polyamino-compounds are oxidized very readily. They are colourless, but many of them are turned brown by oxidation in the air.

Quinone di-imide, $HN{:}C_6H_4{:}NH$, a compound derived from *p*-phenylenediamine, has the same relationship to this amine as benzoquinone to quinol. *Aniline-black* is a complex derivative of this substance, and is formed by the oxidation of aniline. It is a condensation-product of eight molecules of aniline, and is considered to have the constitutional formula

$$C_6H_5\cdot N{:}C_6H_4{:}N\cdot C_6H_4\cdot NH\cdot C_6H_4\cdot NH\cdot C_6H_4\cdot N{:}C_6H_4{:}N\cdot C_6H_4\cdot N{:}C_6H_4{:}NH,$$

indicating union of the eight aniline-residues by nitrogen and not by carbon. One of the arguments in favour of this formula is the almost quantitative conversion of aniline-black by further oxidation into benzoquinone, also an indication of the union of each of the eight aniline-residues with carbon at the *para*-position.

Azo-dyestuffs.

340. The azo-derivatives of the polyamino-compounds are known as *azo-dyestuffs*. They are of great technical importance, being employed extensively in dyeing wool, silk, and cotton. They are azobenzenes with hydrogen atoms replaced by amino-groups. They are not the only dyestuffs, for derivatives of azobenzene with hydrogen replaced by hydroxyl or by the sulpho-group also can be utilized for dyeing. Some of these compounds will be described.

341. Azo-dyestuffs are obtained by the action of diazonium chlorides on aromatic amines or phenols:

$$\underset{\text{Benzene-diazonium chloride}}{C_6H_5\cdot N\cdot Cl} + \underset{\text{Dimethyl-aniline}}{H\cdot C_6H_4\cdot N(CH_3)_2} \rightarrow \underset{\text{Dimethylaminoazobenzene}}{C_6H_5\cdot N=N\cdot C_6H_4\cdot N(CH_3)_2} + HCl;$$

$$\underset{\text{Benzene-diazonium chloride}}{C_6H_5\cdot N\cdot Cl} + \underset{\text{Dihydroxy-benzene}}{H\cdot C_6H_3(OH)_2} \rightarrow \underset{\text{Dihydroxyazobenzene}}{C_6H_5\cdot N=N\cdot C_6H_3(OH)_2} + HCl.$$

Basic or acidic dyestuffs are produced. In 309, mention is made of the possibility of forming a diazoamino-compound as an intermediate product in the combination of a diazonium chloride and an aromatic amine, and of its convertibility into the aminoazo-derivative by warming with the amine hydrochloride. In this formation of aminoazo-compounds and hydroxyazo-compounds, the *para*-hydrogen atom always reacts with the diazonium chloride, for its replacement by a substituent either inhibits the formation of dyestuff, or renders it very incomplete.

The possible variations of this "Coupling method" are very numerous, for nearly every diazonium salt can combine with derivatives of aromatic amines and phenols having most diverse substituents. As a result the number of the azo-dyestuffs is at least as great as the total of all other dyestuffs. They dye not only wool, cotton, and silk, but also linen, paper, and other materials; and they are available in every variety of colour and degree of fastness.

In preparing hydroxyazo-dyestuffs, the solution of the diazonium chloride is cooled with ice, and is added slowly to the *alkaline* solution of the phenol or its sulphonic acid. The reaction-mixture is kept slightly alkaline to prevent the hydrogen chloride liberated hindering the formation of the dyestuff. After the solutions have been mixed, the dyestuff is "salted out" in flocculent masses by the addition of common salt. It is freed from water by means of a filter-press, and packed either as a powder or a paste.

Aminoazo-dyestuffs are prepared by mixing the aqueous solution of the diazonium chloride with that of the aromatic amine salt, the colouring-matter subsequently being salted out. Sometimes it is necessary to employ an alcoholic solution.

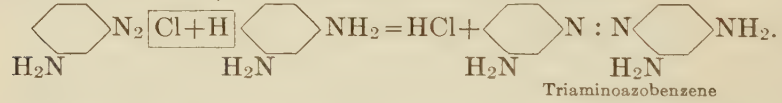
The simplest azo-dyestuffs are yellow. The introduction of alkyl-groups or phenyl-groups, and normally increase of molecular weight, change their colour through orange and red to violet and blue. They are crystalline, and most of them are insoluble in water and soluble in alcohol. Instead of the azo-dyestuffs themselves, it is often better to employ their sulphonic acids, obtainable from them by the usual method with concentrated sulphuric acid.

The best azo-dyestuffs for technical purposes are those produced from naphthalene derivatives. A short account of some of these dyestuffs belonging to the group of benzene derivatives is subjoined.

Aniline-yellow is a salt of aminoazobenzene, but it is seldom used now, its place having been taken by other yellow dyestuffs.

Chrysoidine or *diaminoazobenzene*, $C_6H_5 \cdot N{:}N \cdot C_6H_3 < \begin{matrix} NH_2 \\ NH_2 \end{matrix}$, is obtained from benzenediazonium chloride and *m*-phenylenediamine. It yields a hydrochloride crystallizing in needles of a reddish colour, and fairly soluble in water. This salt dyes wool and silk directly, and mordanted cotton.

Bismarck-brown or *vesuvine* is formed by addition of nitrous acid to an aqueous solution of *m*-phenylenediamine. It is a mixture of various dyestuffs, among them *triaminoazobenzene*, manufactured by diazotizing one of the amino-groups in *m*-phenylenediamine, and bringing the product into contact with a second molecule of that base:



Triaminoazobenzene

Bismarck-brown consists mainly of more complex derivatives, formed by diazotization of both the amino-groups of *m*-phenylenediamine and union of the products with two molecules of that base.

Even a very dilute solution of nitrous acid gives a brown coloration with *m*-phenylenediamine, due to the formation of Bismarck-brown or related substances. This reaction furnishes a very delicate test for nitrous acid, and is employed in water-analysis.

Helianthine or *dimethylaminoazobenzenesulphonic acid* is prepared by the interaction of *p*-sulphobenzenediazonium chloride and dimethylaniline hydrochloride in aqueous solution:

$$HO_3S \cdot C_6H_4 \cdot N_2\boxed{Cl+H}C_6H_4 \cdot N(CH_3)_2 =$$

$$= HCl + \underbrace{HO_3S \cdot C_6H_4 \cdot N{:}N \cdot C_6H_4 \cdot N(CH_3)_2}_{\text{Helianthine}}.$$

It is not utilized much as a dyestuff, but its yellow sodium salt, turned red by acids, is employed as an indicator in volumetric analysis under the name *methyl-orange*.

Resorcin-yellow or *dihydroxyazobenzenesulphonic acid,*

$$HO_3S \cdot C_6H_4 \cdot N{:}N \cdot C_6H_3 < \begin{matrix} OH \\ OH' \end{matrix}$$

is obtained from resorcinol (**336**) and *p*-sulphobenzenediazonium chloride.

The azo-dyestuffs are converted into amino-compounds by energetic reduction with tin and hydrochloric acid, aminoazobenzene yielding aniline and *p*-phenylenediamine:

$$C_6H_5 \cdot N{=}N \cdot C_6H_4 \cdot NH_2 \rightarrow C_6H_5 \cdot NH_2 + C_6H_4 < \begin{matrix} NH_2\,{}^1 \\ NH_2\,{}^4 \end{matrix}.$$

This decomposition by reduction affords a means of determining the constitution of these dyestuffs, and indicates the methods for their preparation. An example is the reduction of a dyestuff with tin and hydrochloric acid to a mixture of equimolecular amounts of diaminobenzene and triaminobenzene, revealing the constitution of the compound to be

$$NH_2 \cdot C_6H_4{-}N{:}\,\vdots\,N{-}C_6H_3 < \begin{matrix} NH_2 \\ NH_2 \end{matrix}.$$

This decomposition also demonstrates the dyestuff to be obtainable by diazotizing a molecule of diaminobenzene, and bringing the product into contact with a second molecule of diaminobenzene, in accordance with the foregoing equation.

VII. SUBSTITUTED BENZOIC ACIDS; POLYBASIC ACIDS AND THEIR DERIVATIVES.

Halogen-benzoic Acids.

342. Direct chlorination, with ferric chloride as catalyst, converts benzoic acid into a complex mixture of acids. The only monochloro-constituent of the product is m-*chlorobenzoic acid,* it being associated with polychloro-acids very difficult to separate. *m*-Chlorobenzoic acid can be obtained also from the corresponding amino-derivative by the diazotization-method, a reaction well adapted to the preparation of the halogen-benzoic acids. The interaction of phosphorus pentachloride and the hydroxybenzoic acids proceeds less smoothly. p-*Chlorobenzoic acid* and p-*bromobenzoic acid* usually are prepared by oxidation of the corresponding halogen-toluenes.

As would be expected, the acidic character of benzoic acid is strengthened by the introduction of halogen. The dissociation-constant 10^4k of the halogen-benzoic acids is greater than that of benzoic acid itself.

For benzoic acid 10^4k is 0·6; for *o*-chlorobenzoic acid 13·2, for *m*-chlorobenzoic acid 1·55; for *p*-chlorobenzoic acid 0·93. These values prove the chlorine atom in the *ortho*-position to exert the greatest influence, and that in the *para*-position the least, while for the *m*-compound 10^4k is intermediate in value.

Nitrobenzoic Acids.

m-*Nitrobenzoic acid* is the principal product obtained by nitrating benzoic acid, about 20 per cent. of o-*nitrobenzoic acid* and a very small proportion of p-*nitrobenzoic* acid being formed simultaneously. The *ortho*-compound is obtained best by the oxidation of *o*-nitrotoluene, and is characterized by an intensely sweet taste.

The introduction of the nitro-group causes a large increase in the value of the dissociation-constant 10^4k. For benzoic acid it is 0·6, for *o*-nitrobenzoic acid 61·6, for the *meta*-acid 3·45, and for the *para*-acid 3·96. The melting-points of these acids in the order named are 148°, 141°, and 241°.

Sulphobenzoic Acids.

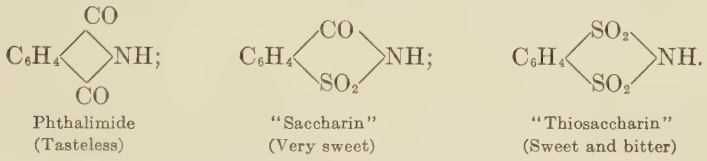
343. o-*Benzoic sulphinide*, $C_6H_4<\begin{matrix}SO_2\\CO\end{matrix}>NH$, the imino-derivative of *o*-sulphobenzoic acid, is known as "saccharin." It is about five hundred times as sweet as sucrose, and on this account is employed sometimes as a substitute for it. It has no dietetic value, being eliminated unchanged from the body. Direct sulphonation of benzoic acid yields m-*sulphobenzoic acid* almost exclusively, a fact rendering the process inapplicable to the preparation of "saccharin." It is obtained from toluene, a substance converted by chlorosulphonic acid, $SO_2(OH)Cl$, into a mixture of p-*toluenesulphonyl chloride* and o-*toluenesulphonyl chloride*, the first being the chief product. The *ortho*-chloride is converted into its *sulphonamide*, the methyl-group of the amide then becoming transformed into carboxyl by oxidation with potassium permanganate. On liberation of this acid from its potassium salt by means of sulphuric acid, one molecule of water is eliminated instantly, forming "saccharin":

$$\underset{\text{Toluene}}{C_6H_5\cdot CH_3} \rightarrow \underset{\text{o-Toluenesulphonyl chloride}}{C_6H_4<\begin{matrix}SO_2Cl\ 1\\CH_3\ \ 2\end{matrix}} \rightarrow C_6H_4<\begin{matrix}SO_2\cdot NH_2\\CH_3\end{matrix} \rightarrow$$

$$\rightarrow \underset{\substack{\text{o-Sulphonamide of}\\\text{benzoic acid}}}{C_6H_4<\begin{matrix}SO_2\cdot NH_2\\COOH\end{matrix}} \rightarrow \underset{\text{"Saccharin"}}{C_6H_4<\begin{matrix}SO_2\\CO\end{matrix}>NH.}$$

"Saccharin" is a white crystalline powder melting at 220°, soluble with difficulty in cold water, and readily soluble in alcohol and ether. It adds one molecule of water, yielding the sulphonamide of *o*-sulphobenzoic acid, a substance lacking a sweet taste.

Little is known as to the relation between taste and chemical structure. The most diverse compounds are characterized by having a sweet taste, for chemically there is no resemblance between "saccharin" and sucrose. On replacing the hydrogen atoms in the benzene-nucleus of "saccharin," the taste usually changes from sweet to bitter. It is interesting that phthalimide is tasteless, "saccharin" is sweet, and the "thiosaccharin" formed by replacing the carbonyl-group of "saccharin" by a sulpho-group is much less sweet, being possessed of an astringent and bitter after-taste:



Phthalimide (Tasteless) — "Saccharin" (Very sweet) — "Thiosaccharin" (Sweet and bitter)

Monohydroxy-acids.

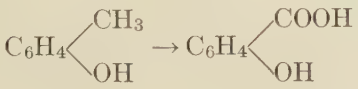
344. The most important of the monohydroxy-acids is o-*hydroxybenzoic acid* or *salicylic acid*, $C_6H_4{<}^{OH}_{COOH}{}^{1}_{2}$. It derives its name from salicin, a glucoside in the bark and leaves of the willow (*salix*). Hydrolysis of this substance yields *saligenin* and dextrose:

$$\underset{\text{Salicin}}{C_{13}H_{18}O_7}+H_2O=\underset{\text{Saligenin}}{C_7H_8O_2}+\underset{\text{Dextrose}}{C_6H_{12}O_6}.$$

Saligenin is the alcohol corresponding with salicylic acid, being converted into it by oxidation:

$$\underset{\text{Saligenin}}{C_6H_4{<}^{OH}_{CH_2OH}}\rightarrow\underset{\text{Salicylic acid}}{C_6H_4{<}^{OH}_{COOH}}.$$

Salicylic acid is present as methyl ester in oil of wintergreen (*Gaultheria procumbens*), sometimes a source of the acid employed in pharmacy. A good yield of the acid is obtained by fusing *o*-cresol with caustic alkali and lead peroxide as an oxidizer:

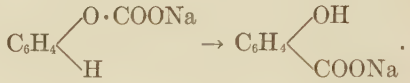


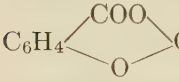
Salicylic acid is manufactured by a process discovered by KOLBE and improved by SCHMIDT, sodium phenoxide being heated with carbon dioxide in an autoclave at 130°.

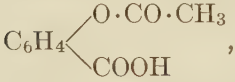
At the ordinary temperature and a pressure of about $1\frac{1}{3}$ atmosphere, sodium phenoxide and carbon dioxide react to form *sodium phenylcarbonate*:

$$C_6H_5\cdot O\cdot Na + CO_2 = C_6H_5\cdot O\cdot COONa.$$

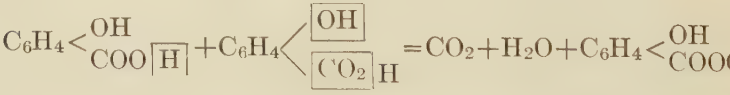
This compound is to be regarded as an intermediate product in the synthesis of salicylic acid. Its conversion into that substance is represented by the scheme



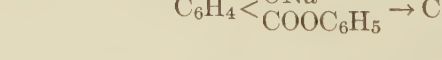
Salicylic acid is a white crystalline powder dissolving with difficulty in cold water, and melting at 159°. Gentle heating effects its sublimation, but strong heating decomposes it into phenol and carbon dioxide. With bromine-water it yields a precipitate of the formula $C_6H_2Br_3\cdot OBr$. It gives a violet coloration with ferric chloride, both in aqueous solution and in alcoholic solution, in contrast with phenol dissolved in alcohol. Boiling a solution of salicylic acid with calcium chloride and ammonia precipitates the basic calcium salicylate,  , a reaction affording a means of separating salicylic acid from its isomerides, for with these reagents they do not give a correponding basic salt.

Salicylic acid is a powerful antiseptic, and is employed as a preservative for foods and such beverages as beer, although not completely innocuous. Sodium salicylate and the acetyl-derivative, "aspirin,"  , are utilized in medicine.

Heating the acid at 220° eliminates carbon dioxide and water, forming *phenyl salicylate*:



This compound is employed as an antiseptic under the name "salol." At 300°, its sodium derivative is converted into *sodium phenylsalicylate*:



m-*Hydroxybenzoic acid* and p-*hydroxybenzoic acid* do not yield a coloration with ferric chloride. Their basic barium salts are insoluble.

Dihydroxy-acids.

Among the *dihydroxy-acids* is *protocatechuic acid*, C_6H_3(COOH 1, OH 3, OH 4).

It is obtained from many resins by fusion with potassium carbonate; and it is synthesized by heating catechol with ammonium carbonate, a method furnishing a striking example of the readiness sometimes characteristic of the introduction of the carboxyl-group into the ring. It is freely soluble in water. It reduces an ammoniacal silver solution, but not an alkaline copper solution. It gives a characteristic reaction with ferric chloride, yielding a green colour changing to blue and finally to red on addition of a very dilute solution of sodium carbonate.

Trihydroxy-acids.

345. The best-known *trihydroxy-acid* is *gallic acid*,

C_6H_2(COOH 1, OH 3, OH 4, OH 5).

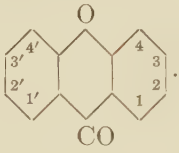
It is a constituent of gall-nuts, tea, and " divi-divi," a material employed in tanning. It is prepared usually by boiling tannin with dilute acids. It crystallizes in fine needles readily soluble in hot water. Mention is made in 337 of the effect of heat, the acid losing carbon dioxide, and forming pyrogallol. Gallic acid reduces the salts of gold and silver, and gives a bluish-black precipitate with ferric chloride. Like pyrogallol, in alkaline solution it is turned brown in the air by oxidation.

Gallic acid is employed in the manufacture of one form of blue-black ink. For this purpose its aqueous solution is mixed with a solution of ferrous sulphate containing a trace of free sulphuric acid. Without the acid, the ferrous sulphate would oxidize quickly in the air, giving a thick black precipitate with the gallic acid. This oxidation is retarded in a remarkable manner by the addition of a very small proportion of sulphuric acid. On contact with paper, the aluminium oxide present neutralizes the free acid, and oxidation being prevented no longer, the writing dries to a deep black. As the mixture of the solutions of ferrous sulphate and gallic acid has only a faint-brown colour, indigo-carmine is added to the mixture to make the fresh writing more visible. This dyestuff imparts to the ink left by the pen a dark-blue colour, and it changes by the process described to a deep black.

Vegetable Dyestuffs and Tannins.

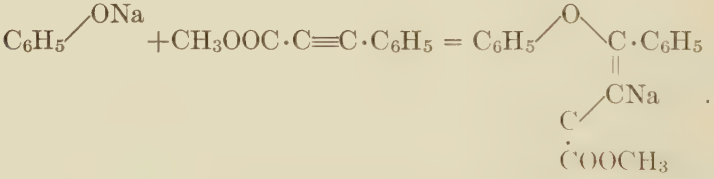
346. The various *vegetable dyestuffs* and *tannins* are very important natural products related to the hydroxybenzoic acids.

A considerable proportion of the vegetable dyestuffs are connected with salicylic acid, most of them being characterized by a yellow colour. They are classified in two groups, the *xanthones* and *flavones*, and have been investigated mainly by VON KOSTANECKI. Distillation of salicylic acid with acetic anhydride yields first the phenyl ether of salicylic acid, $C_6H_4{<}^{OC_6H_5}_{COOH}$, a substance further converted by elimination of water into *xanthone*,

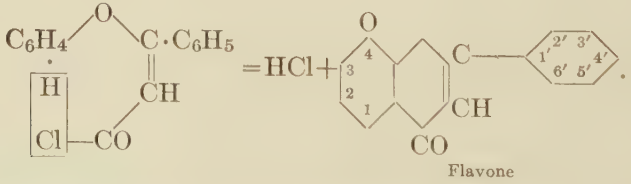


Euxanthone or *Indian yellow* is a dihydroxy-derivative of xanthone, with a hydroxyl-group in each benzene-nucleus.

Flavone is formed by the condensation of methyl phenylpropiolate and sodium phenoxide:



Saponification of this intermediate product and replacement of sodium by hydrogen yield the corresponding unsaturated acid. The chloride of this acid condenses quantitatively to flavone under the influence of aluminium chloride:



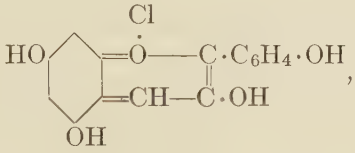
Flavone

Among the flavones are *chrysin* or 1:3-dihydroxyflavone, the yellow dyestuff of poplar buds; *luteolin* or 1:3:3′:4′-tetrahydroxy-

flavone, the colouring matter of dyers' weld (*Reseda luteola*); and *morin* or 1:3:2′:4′-*tetrahydroxyflavone*, the dyestuff of mulberry (*Morus tinctoria*); and other products.

Willstätter's remarkable researches on the colouring principles of flowers and fruits have identified among the constituents of these substances *p*-hydroxybenzoic acid, protocatechuic acid, and gallic acid. These colouring matters are glucosides, and have the name *anthocyanins*. Their extraction from the plants is facilitated by the formation of well-crystallized salts with mineral acids and also with organic acids. As the anthocyanins do not contain nitrogen, Willstätter regards these salts as oxonium derivatives (239).

Heating with hydrogen chloride decomposes the anthocyanins into carbohydrate and the characteristic colour-components, known as *anthocyanidins*. Investigation of anthocyanidins derived from a great variety of coloured flowers and fruits has led to a surprising conclusion as to all of them containing the same atomic grouping combined with the three acids cited previously. The oxonium salts formed with hydrogen chloride have a structure of the type



the group $\equiv C \cdot C_6H_4 \cdot OH$ derived from *p*-hydroxybenzoic acid being replaceable by $\equiv C \cdot C_6H_3(OH)_2$ from protocatechuic acid, or by $\equiv C \cdot C_6H_2(OH)_3$ from gallic acid. The variegated wealth of colour displayed by flowers is due partly to the union of these compounds with acids to form oxonium salts, and partly to their combination with bases to produce phenoxides, all these derivatives having different characteristic colours.

The blue colour of the corn-flower is caused by an alkali-metal salt of an anthocyanin identical with that imparting its colour to the rose and geranium in the form of red oxonium salt. Lichens also contain characteristic colouring matters, and some of these products have been synthesized from hydroxy-acids. Emil Fischer prepared from these acids a lengthy series of derivatives of this type, and gave them the collective name *depsides* (δέψειν, tan). The number of phenolcarboxylic acid-residues in the molecule is indicated by a Greek prefix, di-, tri-, tetra-depsides, and so on, being known.

Syntheses of this type are exemplified by the formation of the

didepside of *p*-hydroxybenzoic acid. In alkaline solution, acetyl chloride and this acid react in accordance with the equation

$$CH_3 \cdot COCl + NaO \cdot C_6H_4 \cdot COONa = CH_3 \cdot CO \cdot OC_6H_4 \cdot COONa + NaCl.$$

Acetyl chloride

The phenolic hydroxyl of the *p*-hydroxybenzoic acid being rendered inactive, the acid can be converted into its chloride by means of phosphorus pentachloride, and the product caused to react in alkaline solution with a second molecule of the acid:

$$CH_3 \cdot CO \cdot O \cdot C_6H_4 \cdot COCl + NaO \cdot C_6H_4 \cdot COONa = \\ = CH_3 \cdot CO \cdot OC_6H_4 \cdot CO \cdot OC_6H_4 \cdot COONa + NaCl.$$

Saponification replaces the acetyl-group, $CH_3 \cdot CO—$, by hydrogen, forming the didepside,

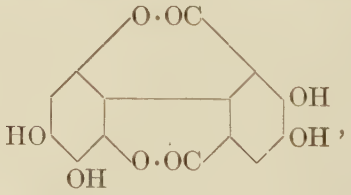
$$HO \cdot C_6H_4 \cdot CO \cdot OC_6H_4 \cdot COOH.$$

Many flowers, and other parts of plants such as the leaves in autumn, have a yellow or orange colour. This characteristic is due to the presence of the yellow colouring matter of carrots (*Daucus carota*), known as *carrotene*. It is a hydrocarbon of the formula $C_{26}H_{38}$.

347. The *tannins* or *tannic acids* are distributed very widely throughout the vegetable kingdom. They are soluble in water, have a bitter astringent taste, yield a dark-blue or green precipitate with ferric salts, convert animal hides into leather, and precipitate proteins from their solutions.

Three groups of tannins are recognized. Most of these substances are related to the tannin obtained from oak-bark. They are connected also with *catechin*, a white crystalline substance of known structure, the principal constituent of *gambier*, a tannin material found in Sumatra and related to the anthocyanidins. These tannins give a red coloration with acids.

A second group of tannins comprises those converted by the action of warm dilute acids into *ellagic acid*. This substance has the constitution



and therefore is a depside.

The constitution of the tannins of these two groups is imperfectly understood. The small proportion of tannins belonging to the third group includes an important compound, the *tannin* of gall-nuts. The constitution of this substance has been elucidated almost completely by analysis and synthesis. Warming with dilute sulphuric acid adds the elements of water, decomposing this tannin into gallic acid and dextrose. From these two compounds Emil Fisher synthesized *pentadigalloylglucose*,

$$\underset{\text{Dextrose residue}}{C_6H_7O_6}[\underset{\text{Digalloyl-residue}}{C_6H_2(OH)_3\cdot CO\cdot OC_6H_2(OH)_2\cdot CO}]_5 \quad \text{or} \quad C_{76}H_{52}O_{46},$$

a substance displaying very great analogy to tannin. The first step in the process is the conversion of gallic acid into a didepside, *galloylgallic acid*,

$$(HO)_3C_6H_2\cdot CO\cdot OC_6H_2\begin{cases}OH\\OH\\COOH\end{cases},$$

the chloride of this acid reacting with dextrose to form pentadigalloylglucose. Tannin is probably a mixture of substances analogous to pentadigalloylglucose.

Tannin imparts its characteristic bitter taste to many beverages, an example being over-infused tea. The addition of milk removes this bitter taste, because the tannin forms an insoluble compound with the proteins present in the milk.

Tannin is a white, sometimes yellowish, amorphous powder, readily soluble in water, only slightly soluble in alcohol, and insoluble in ether. It forms salts with two equivalents of the metals, and precipitates many alkaloids, such as strychinine and quinine, from their aqueous solutions (407). It is probably a mixture of compounds analogous to pentadigalloylglucose.

The tannins find application in medicine and in the tanning of hides.

In making leather, the hide is saturated with the tannin, because otherwise it cannot be employed in the manufacture of shoes and other articles, for it dries soon to a hard horn-like substance, or in the moist condition becomes rotten. When saturated with tannin it remains pliant, and does not decompose.

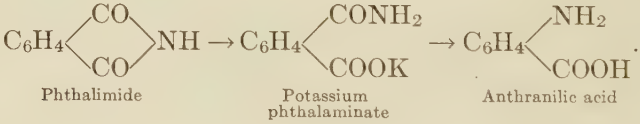
The skin of an animal consists of three layers, the epidermis, the cuticle, and the fat. The cuticle being the part made into leather, decomposition of the epidermis and the fat is induced by suspending the hides in running water, these layers being removed subsequently by means of a blunt knife. Alternate horizontal layers of the hides thus prepared and oak-bark or some

other material containing tannin are placed in large troughs or vats, and these containers are filled with water. At the end of six or eight weeks the hides are taken out and placed in a second vat containing fresh bark of stronger quality. This procedure is continued with successive batches of tan-liquor of increased concentration, until the hides are tanned perfectly, the process lasting as long as two or three years, according to the thickness of the hide. The completion of the tanning of a hide can be judged from the appearance of its cross-section, or by the aid of dilute acetic acid. Internal swelling due to contact with the acid indicates the conversion into leather to be incomplete.

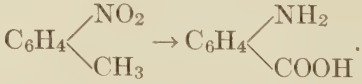
The process of tanning probably involves a mutual precipitation of colloids. The hide contains proteins in the form of gels ("Inorganic Chemistry," 192), and the tanning material dissolves in them as a colloid dissolves in water. Among the reasons for this assumption is the fact of the freezing-point of the solvent remaining unaltered. At first the tanning material simply is absorbed by the hide, for it can be extracted by water. After the tanning process has continued for some time, there is a diminution in the proportion extracted.

Aminobenzoic Acids.

The most important of the *aminobenzoic acids* is o-*aminobenzoic acid* or *anthranilic acid*, first produced by the oxidation of indigo (404). It has the character of an amino-acid, yielding salts with both acids and bases. It possesses a sweet taste and slightly antiseptic properties. It is obtained by the method of Hoogewerff and van Dorp (259), by the action of phthalimide on bromine and potassium hydroxide. The potassium salt of phthalaminic acid is the initial product, and changes to anthranilic acid:



By a very interesting intramolecular rearrangement, *o*-nitrotoluene is transformed into anthranilic acid by a boiling alkaline solution:



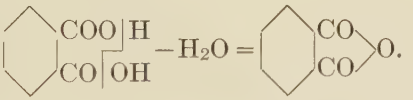
Anthranilic acid melts at 145°, and by heating gently it can be sublimed without decomposition. Stronger heating decomposes it to a considerable extent into carbon dioxide and aniline. It dissolves in

water and readily in alcohol. By the method indicated it is prepared technically for the synthesis of indigo, bleaching-powder being substituted for the potassium hydroxide and bromine. Its methyl ester causes the fragrance of many flowers; and as it has a powerful, but agreeable, odour, it finds application in the perfume-industry.

Phthalic Acid.

348. *Phthalic acid* is the *ortho*-dicarboxylic acid of benzene, and has the formula $C_6H_4{<}^{COOH\ 1}_{COOH\ 2}$. It is obtained by the oxidation of aromatic hydrocarbons with two side-chains in the *ortho*-position, or of their derivatives with substituents in the side-chains. Chromic acid cannot be employed in this oxidation, for it decomposes *ortho*-derivatives completely into carbon dioxide and water. Phthalic acid is employed in the preparation of artificial indigo (405), and is manufactured by oxidizing naphthalene (377), $C_{10}H_8$, with air at 400°–500°, vanadium pentoxide being employed as a catalyst.

Phthalic acid is crystalline, and dissolves readily in hot water, alcohol, and ether. It has no definite melting-point, for heating eliminates water, and yields a sublimate of *phthalic anhydride* in beautiful long needles:



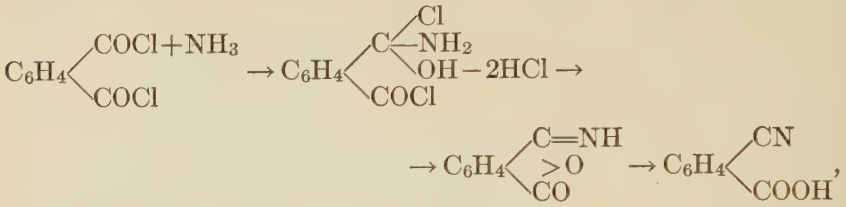
Phthalic anhydride

Phthalyl chloride is made by the interaction of phosphorus pentachloride and phthalic acid. It exists in two tautomeric forms,

I. II.

The first form is produced by direct interaction of the chloride and the acid, and is transformed into the second modification by warming with aluminium chloride. Form II is converted very readily into I. There is a marked divergence in melting-point, I melting at 16°, and II at 89°. With ammonia and aniline I reacts much more rapidly than II, although in these and various other reactions identical substances are produced from the two tautomerides. An example is the formation of cyano-

benzoic acid under the influence of ammonia, as indicated in the scheme



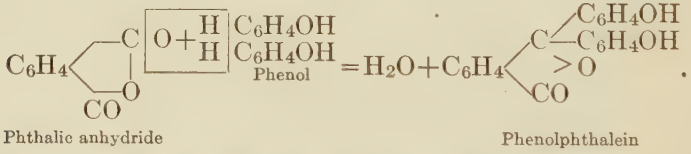
while the *iso*-chloride reacts thus:

$$>CCl_2+H_2NH \rightarrow >C{=}NH.$$

This similarity in behaviour has made it extremely difficult to solve by purely chemical methods the problem of the correct constitutional formula of each isomeride.

The results of optical research indicate the great probability of the product directly produced having formula I. Chlorine atoms in immediate union with a carbonyl-group, $>CO$, have a higher atomic refraction than chlorine atoms otherwise attached to carbon. The atomic refraction of O″ is also greater than that of $<O$. A compound with constitution I must therefore have a higher molecular refraction than one with structure II, and the value found experimentally for the direct product melting at 16° is higher than that of the substance melting at 89°.

The oxygen of the carbonyl-group in phthalic anhydride can participate also in other reactions, heating that substance with phenols and sulphuric acid forming *phthaleins*:

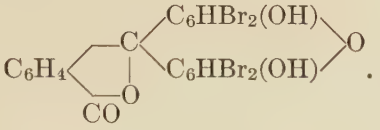


Phthalic anhydride — Phenol — Phenolphthalein

Phenolphthalein, the simplest member of the phthalein series, is a yellow powder. On account of its phenolic character it dissolves in alkaline solutions, with formation of a fine red colour, and is a sensitive indicator for alkalimetry (**374**).

Resorcinolphthalein or *fluorescein* is characterized by the display of an intense yellowish-green fluorescence in alkaline solution. It owes its name to this property, and the reaction affords a delicate test for phthalic anhydride, phthalic acid, and resorcinol, fluorescence being exhibited by mere traces of fluorescein. It is prepared by heating a

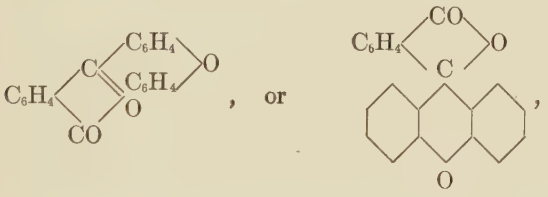
mixture of resorcinol and phthalic anhydride at 210°, in presence of zinc chloride as a dehydrator. Bromine converts fluorescein into *tetrabromofluorescein*:



Its potassium derivative, $C_{20}H_6O_5Br_4K_2$, is the beautiful dye *eosin*.

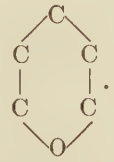
The constitution of the phthaleins is inferred from their convertibility into derivatives of triphenylmethane (**373**).

In the preparation of phenolphthalein the by-product *fluoran*, insoluble in alkalis, is produced. This substance has the formula

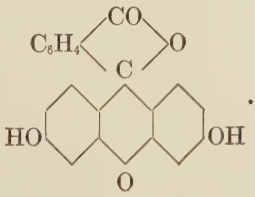


I. II.

the two phenol-residues being united at the *ortho*-positions to the phthalic-anhydride-residue, and not at the *para*-positions as in phenolphthalein. Fluoran contains the pyrone-nucleus,



Many derivatives containing this nucleus fluoresce. Fluorescein is dihydroxyfluoran, with the formula



349. *Phthalimide*, $C_6H_4\begin{<}CO\\CO\end{>}NH$, is of importance on account of its application to the synthesis of primary amines with substituted alkyl-groups. It is obtained by passing dry ammonia over heated phthalic anhydride. The imino-hydrogen is replaceable by metals, the potassium compound being precipitated by the action of potassium hydroxide on the alcoholic solution of the imide. When *potassium phthalimide* reacts with an alkyl halide, the metal becomes replaced by alkyl; and heating the product with acids or alkalis yields a primary amine free from secondary and tertiary amines:

$$C_6H_4\begin{<}CO\\CO\end{>}N\boxed{K+Br}\cdot C_nH_{2n+1} \rightarrow C_6H_4\begin{<}CO\\CO\end{>}N\cdot C_nH_{2n+1} \rightarrow$$

Potassium phthalimide

$$\rightarrow C_6H_4<\begin{matrix}COONa\\COONa\end{matrix}+NH_2\cdot C_nH_{2n+1}.$$

Alkyl halides with various substituents can be employed in this reaction. From ethylene bromide, $CH_2Br\cdot CH_2Br$, there is obtained *bromoethylamine*, $NH_2\cdot CH_2\cdot CH_2Br$; from ethylenebromohydrin, $CH_2Br\cdot CH_2OH$, *aminoethyl alcohol* or *hydroxyethylamine*, $NH_2\cdot CH_2\cdot CH_2OH$; etc. Colamine is considered in **160**.

Another example is Emil Fischer's synthesis of *ornithine* (**243**). Potassium phthalimide is brought into contact with trimethylene bromide:

$$C_6H_4<\begin{matrix}CO\\CO\end{matrix}>N\boxed{K+Br}\cdot CH_2\cdot CH_2\cdot CH_2Br \rightarrow$$

$$\rightarrow C_6H_4<\begin{matrix}CO\\CO\end{matrix}>N\cdot CH_2\cdot CH_2\cdot CH_2Br.$$

The compound obtained reacts with diethyl monosodiomalonate to yield $C_6H_4<\begin{matrix}CO\\CO\end{matrix}>N\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(COOC_2H_5)_2$, its tertiary hydrogen atom then being replaced by bromine. Saponification, and elimination of carbon dioxide, give

$$C_6H_4<\begin{matrix}CO\\CO\end{matrix}>N\cdot CH_2\cdot CH_2\cdot CH_2\cdot CHBr\cdot COOH.$$

Heating with aqueous ammonia replaces the bromine atom by the

amino-group. Subsequent heating with concentrated hydrochloric acid yields ornithine:

$$C_6H_4 < \begin{matrix} CO \\ CO \end{matrix} > N \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot COOH = \\ +2OHH$$

$$= C_6H_4 < \begin{matrix} COOH \\ COOH \end{matrix} + H_2N \cdot CH_2 \cdot CH_2 \cdot \underset{\text{Ornithine}}{CH_2 \cdot CH(NH_2)} \cdot COOH.$$

These examples demonstrate the applicability of this method to the preparation of primary amines with a great variety of substituents.

Metaphthalic and Terephthalic Acids, $C_6H_4(COOH)_2$(1:3) and (1:4).

350. *Metaphthalic acid* can be obtained by the oxidation of compounds with two side-chains in the *meta*-position, and also by the oxidation of resin (colophonium) with nitric acid. It dissolves with difficulty in water, and does not yield an anhydride.

Terephthalic acid can be prepared by several methods, an example being the oxidation of turpentine. It is almost insoluble in water, alcohol, and ether. It does not melt at the ordinary pressure, but at high temperatures it sublimes without decomposition. Like metaphthalic acid, it does not form an anhydride.

Higher Polybasic Acids.

Tricarboxylic, tetracarboxylic, pentacarboxylic, and hexacarboxylic acids are known. The most remarkable is the hexacarboxylic *mellitic acid*, a constituent of the mineral *honey-stone*, found in brown-coal seams. Honey-stone is the aluminium salt of mellitic acid, and has the formula

$$C_{12}O_{12}Al_2,18H_2O.$$

It forms yellow quadratic octahedra. Mellitic acid is produced by the oxidation of wood-charcoal with an alkaline solution of potassium permanganate. It crystallizes in fine needles, and dissolves freely in water and alcohol. Heating expels from it two molecules of carbon dioxide and two molecules of water, with formation of *pyromellitic anhydride*,

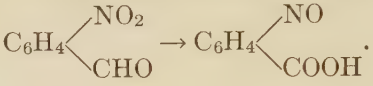
$$C_6H_2 \begin{matrix} \diagup CO \\ \diagup CO \end{matrix} > O \begin{matrix} 1 \\ 2 \end{matrix} \\ \diagdown CO \\ \diagdown CO \end{matrix} > O \begin{matrix} 4 \\ 5 \end{matrix}.$$

This substance adds water, yielding *pyromellitic acid*, $C_6H_2(COOH)_4$.

VIII. SUBSTITUTED ALDEHYDES.

351. m-*Nitrobenzaldehyde* is the main compound formed in the nitration of benzaldehyde, 20 per cent. of o-*nitrobenzaldehyde* being a

by-product in the reaction. The best mode of preparing the *ortho*-compound is to oxidize *o*-nitrotoluene with manganese dioxide and sulphuric acid. In sunlight it is transformed rapidly into o-*nitrosobenzoic acid:*



Hydroxyaldehydes.

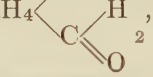
Hydroxyaldehydes can be obtained artificially by a synthetic method generally applicable to the preparation of aromatic hydroxyaldehydes. It consists in bringing the phenols in ethereal solution into contact with anhydrous hydrogen cyanide and hydrogen chloride, it being an advantage sometimes to add a small proportion of zinc chloride as a condensing agent. This mode of synthesis was discovered by Gattermann, and bears his name. The hydrochloride of an imide is formed as an intermediate product, and sometimes can be isolated:

$$C_6H_5OH+HCN+HCl=C_6H_4<\begin{matrix}OH\\CH:NH,HCl\end{matrix}.$$

Warm water converts the imide-salt into the hydroxyaldehyde and ammonium chloride:

$$C_6H_4<\begin{matrix}OH\\CH:NH,HCl\end{matrix}+H_2O=C_6H_4<\begin{matrix}OH\\CHO\end{matrix}+NH_4Cl.$$

In this example p-*hydroxybenzaldehyde* is obtained from phenol.

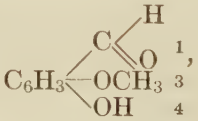
Salicylaldehyde,  , occurs in the volatile *oil of spiræa*.

It can be prepared artificially by Tiemann and Reimer's synthesis, another reaction applicable generally to the production of aromatic hydroxyaldehydes, and dependent on the action of chloroform and potassium hydroxide on phenols:

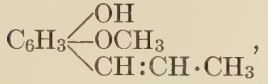
Salicylaldehyde

The *o*-hydroxyaldehydes colour the skin deep yellow.

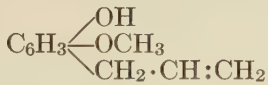
To this class of substances belongs *vanillin*,



the methyl ether of protocatechualdehyde. It is the aromatic principle of vanilla, and is manufactured by oxidizing iso*eugenol*,

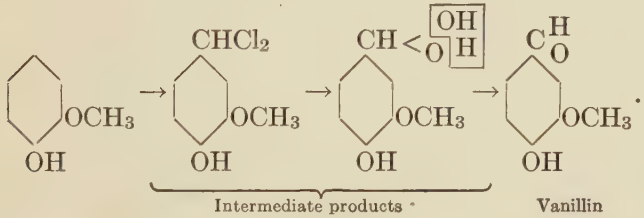


with ozone. *iso*Eugenol is obtained by boiling *eugenol*,



with alcoholic potassium hydroxide, the position of the double bond in the side-chain undergoing transposition. Eugenol is the chief constituent of oil of cloves.

Vanillin has been synthesized by REIMER's method, the action of chloroform and sodium hydroxide on guaiacol (336):



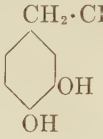
Piperonal is mentioned in 353.

IX. POLYSUBSTITUTED BENZENE DERIVATIVES WITH SUBSTITUENTS IN THE SIDE-CHAIN.

352. p-*Hydroxyphenylpropionic acid*, $C_6H_4<^{OH}_{CH_2\cdot CH_2\cdot COOH}$, is of some importance owing to its relationship with *tyrosine*, a substance melting at 235°, and named from its presence in old cheese (τυρός). It is produced by boiling proteins such as white of egg, horn, and hair with hydrochloric acid or sulphuric acid. Its empirical formula is $C_9H_{11}O_3N$, and its structural formula is $HO\cdot C_6H_4\cdot CH_2\cdot C<^{H}_{NH_2}{}^{COOH}$, it being the 1-amino-acid of *p*-hydroxyphenylpropionic acid. Being an amino-acid, it yields salts with acids as well as with bases.

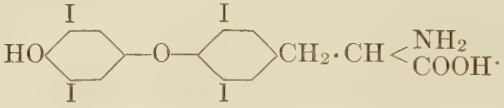
The oxidation of tyrosine under the influence of the enzyme *tyrosinase* yields very stable red, brown, or black colouring matters, the *melanins*.

The colour of the hair of the higher animals and of man, and the dark colour of negroes, originate in an enzymatic oxidation of 3:4-dihydroxyphenylalanine,



This substance can be isolated from the pods of the horse-bean (*Vicia faba*).

Thyroxine is the active principle of the thyroid gland, an organ subject to the disease termed goitre. It is an iodo-derivative of tyrosine with the formula



The synthesis of thyroxine has been effected by HARINGTON.

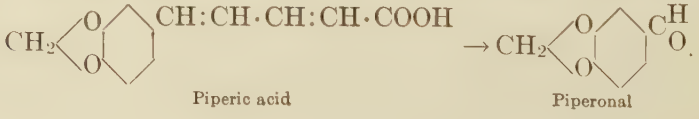
o-*Hydroxycinnamic acid*, $C_6H_4{<}^{OH}_{CH:CH\cdot COOH}$, exists in two forms easily converted into each other, *coumaric acid* and *coumarinic acid*. The second acid is not known in the free state, but only in the form of salts, for its liberation is attended by simultaneous loss of a molecule of water and production of the anhydride *coumarin*, the aromatic principle of woodruff (*Asperula odorata*). Coumaric acid differs in not yielding a corresponding anhydride, removal of water giving coumarin, a substance convertible into salts of coumarinic acid by the action of alkalis.

Coumarin can be obtained from salicylaldehyde by a method analogous to SIR WILLIAM PERKIN'S synthesis (328). Acetylcoumaric acid,

$$C_6H_4{<}^{O\,|\,C_2H_3O}_{CH:CH\cdot CO\,|\,OH},$$

is the initial product, and by heating is converted into coumarin, acetic acid being eliminated.

353. The unsaturated *piperic acid*, or 3:4-*methylenedihydroxycinnamenylacrylic acid*, $C_{12}H_{10}O_4$, is a decomposition-product of piperine (390). Oxidation converts piperic acid into *piperonal* or *heliotropin*,



Piperic acid

Piperonal

The constitution of this substance is established by its synthesis by the action of methylene iodide and alkali on protocatechualdehyde,

$$\begin{matrix}HO\\HO\end{matrix}>C_6H_3\cdot C\overset{H}{\underset{O}{}}.$$

Piperonal melts at 37°, boils at 263°, and has an odour exactly resembling that of heliotropes. In presence of sodium hydroxide piperonal condenses with acetaldehyde to *piperonylacraldehyde*:

$$CH_2<\overset{O}{\underset{O}{}}>C_6H_3\cdot C\overset{H}{\underset{O}{}}+CH_3\cdot C\overset{H}{\underset{O}{}}=$$

$$=CH_2<\overset{O}{\underset{O}{}}>C_6H_3\cdot CH{:}CH\cdot C\overset{H}{\underset{O}{}}+H_2O.$$

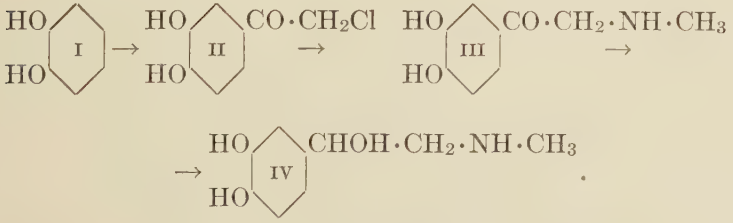
By Perkin's synthetic method (**328**), piperonylacraldehyde is converted by the action of sodium acetate and acetic anhydride into piperic acid:

$$CH_2<\overset{O}{\underset{O}{}}>C_6H_3\cdot CH{:}CH\cdot C\overset{H}{\underset{O}{}}+CH_3\cdot COOH=$$

$$=CH_2<\overset{O}{\underset{O}{}}>C_6H_3\cdot CH{:}CH\cdot CH{:}CH\cdot COOH+H_2O.$$

Adrenaline or *suprarenine*, $C_9H_{13}ON$, is prepared from the suprarenal capsules of the horse and other animals. It is characterized by its powerful hæmostatic properties. Its oxidation yields protocatechuic acid, and distillation with sodium hydroxide gives methylamine. With benzoyl chloride it forms a tribenzoyl-derivative.

It is prepared by a synthetic method. Chloroacetyl chloride reacts with catechol (I) to form *chloroacetylcatechol* (II). With methylamine this substance yields an aminoketone (III), reducible to adrenaline (IV):



Adrenaline

Many organic bases of phenolic character have valuable pharmacological properties. Other types of this class are *hordenine*,

$$\overset{4}{\mathrm{HO}}\cdot\mathrm{C_6H_4}\cdot\overset{1}{\mathrm{CH_2}}\cdot\mathrm{CH_2}\cdot\mathrm{N(CH_3)_2},$$

a substance present in germinating barley; and *tyramine*, the active principle of ergot. The structure of tyramine is established by its formation from tyrosine by the action of heat, carbon dioxide being eliminated:

$$\mathrm{HO}\cdot\mathrm{C_6H_4}\cdot\mathrm{CH_2}\cdot\mathrm{CH(NH_2)}\cdot\mathrm{COOH}-\mathrm{CO_2}\rightarrow\underset{\text{p-Hydroxyphenylethylamine}}{\mathrm{HO}\cdot\mathrm{C_6H_4}\cdot\mathrm{CH_2}\cdot\mathrm{CH_2}\cdot\mathrm{NH_2}}.$$

ORIENTATION OF AROMATIC COMPOUNDS.

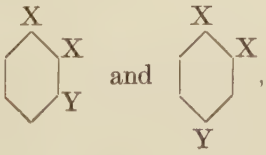
354. *Orientation* is the determination of the relative positions occupied by the side-chains or substituents in the benzene-ring. A description of a number of the more important substitution-derivatives of benzene having been given in the foregoing pages, it becomes necessary to furnish an insight into the methods of orientation. These methods are based on two main principles.

1. *Relative determination of position.*—The compound with substituents in unknown positions is converted into another with known positions, the first compound being inferred to have its substituents arranged similarly to the second. To ascertain the constitution of a substance such as one of the three xylenes involves oxidation of the hydrocarbon. The particular phthalic acid formed indicates the positions of the methyl-groups in the xylene under examination, provided the positions of the carboxyl-groups in the three phthalic acids be known.

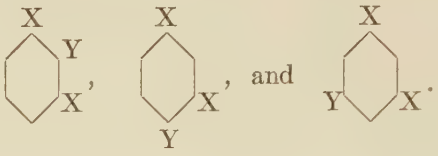
To apply this method, it is necessary to know the positions of the substituents in a small number of compounds, and further the substituents are assumed to retain their positions during the course of the reactions involved. Normally, such continuity holds, although the position of the side-chain does alter in a few reactions (**332** and **333**). To avoid erroneous conclusions from doubtful evidence, sometimes it is desirable to check the determination of position by converting the substance into another compound.

2. *Absolute determination of position.*—The positions of the substituents are determined without the aid of other compounds having substituents in known positions. A general method is afforded by KÖRNER'S *principle*, a rule rendering it possible to ascertain whether substances $C_6H_4X_2$, containing two substituents, are *ortho*-compounds, *meta*-compounds, or *para*-compounds. The mode of procedure is to determine the number of trisubstitution-products corresponding with the substance under investigation.

Introduction of a third group, Y, into an *ortho*-compound, $C_6H_4X_2$, can form two isomerides only,



irrespective of identity or difference of X and Y. The introduction of a third group into a *meta*-compound renders possible the formation of three isomerides,



With a *para*-compound the introduction of a third group yields only one trisubstitution-product,

In addition to this general procedure, some of the other special methods are described in the sequel. They substantiate fully the conclusions based on KÖRNER's principle.

1. Absolute Determination of Position for *ortho*-Compounds.

355. In the *ortho*-series, the structure of a dibromobenzene melting at 5·6° has been determined by means of KÖRNER's principle, for it yields two isomeric nitrodibromobenzenes. The constitution of a *xylene* boiling at 142° and melting at −28° also has been established by this method, it reacting with nitric acid to give two isomeric nitroxylenes. This xylene is converted into phthalic acid by oxidation, proving that acid to be an *ortho*-compound.

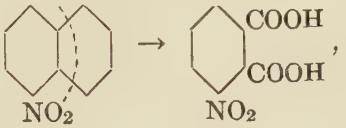
The oxidation of naphthalene (**377**), $C_{10}H_8$, to phthalic acid also demonstrates the carboxyl-groups of that acid to be in the *ortho*-position. This reaction indicates the structure of naphthalene to be $C_6H_4{<}C_4H_4$, the group C_4H_4 being attached to two positions of the benzene-ring. With nitric acid naphthalene forms nitronaphthalene, a substance converted by oxidation into nitrophthalic acid. The group C_4H_4 therefore has become transformed into two carboxyl-groups:

$$\underset{\text{Nitronaphthalene}}{NO_2\cdot C_6H_3{<}C_4H_4} \rightarrow \underset{\text{Nitrophthalic acid}}{NO_2\cdot C_6H_3{<}\begin{matrix}COOH\\COOH\end{matrix}}.$$

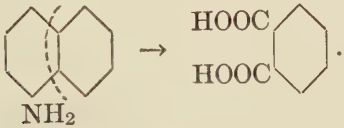
Reduction of the nitro-group, followed by oxidation of the aminonaphthalene, gives phthalic acid, indicating the group C_4H_4 to form a second

benzene-ring with the two carbon atoms of the benzene-ring, and naphthalene to have the formula

The oxidation of nitronaphthalene and that of aminoaphthalene are represented by the schemes



and

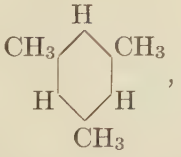


Phthalic acid must, therefore, be an *ortho*-compound, because if it had the *meta*-structure, for example, naphthalene would have the formula

and such an assumption would involve a contradiction, as under these conditions a benzene derivative could not be produced by the oxidation of *both* nitronaphthalene and aminonaphthalene.

2. Absolute Determination of Position for *meta*-Compounds.

356. The proof of mesitylene being symmetrical trimethylbenzene (1:3:5) was enunciated by LADENBURG. If this compound have the constitution



the three hydrogen atoms directly united with the benzene-ring must be of equal value. Proof of this equality would establish the structure of mesitylene.

Ladenburg demonstrated the existence of equality as follows. Nitration of mesitylene yields a dinitro-compound, and if the hydrocarbon be represented by

$$\text{I.}\quad C_6(CH_3)_3\overset{a}{H}\overset{b}{H}\overset{c}{H},$$

this derivative can be assumed arbitrarily to be

$$\text{II.}\quad C_6(CH_3)_3\overset{a}{N}O_2\overset{b}{N}O_2\overset{c}{H}.$$

One of the nitro-groups of the dinitro-compound is reduced, and the amino-compound is converted into an acetyl-derivative assumed to be

$$\text{III.}\quad C_6(CH_3)_3\overset{a}{N}O_2(N\overset{b}{H}C_2H_3O)\overset{c}{H}.$$

This substance can be nitrated again, and the product must be

$$C_6(CH_3)_3\overset{a}{N}O_2(N\overset{b}{H}C_2H_3O)\overset{c}{N}O_2.$$

It is possible to eliminate the acetylamino-group, $NH(C_2H_3O)$, from this derivative by saponification, subsequent diazotization, etc., a dinitro-mesitylene with the formula

$$C_6(CH_3)_3\overset{a}{N}O_2\overset{b}{H}\overset{c}{N}O_2$$

being obtained. It is identical with the original dinitro-product with its nitro-groups at *a* and *b*. Consequently, $H^b = H^c$.

Nitromesidine, *a*:*b*, has an acetyl-compound represented by formula III, and furnishes a further proof of the equality H^a and H^c. Elimination of the amino-group by the diazo-reaction gives a product of formula IV:

$$\text{IV.}\quad C_6(CH_3)_3\overset{a}{N}O_2\overset{b}{H}\overset{c}{H}.$$

This substance is reduced, and is converted into the acetyl-compound acetylmesidine,

$$C_6(CH_3)_3N\overset{a}{H}(C_2H_3O)\overset{b}{H}\overset{c}{H}.$$

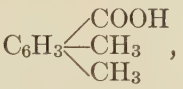
It also can be nitrated, yielding

$$C_6(CH_3)_3N\overset{a}{H}(C_2H_3O)\overset{b}{N}O_2\overset{c}{H}.$$

It is immaterial whether the nitro-group of this compound is at *b* or *c*, the equality of these positions relative to *a* having been proved already.

Elimination of the acetylamino-group from the last substance gives a mononitromesitylene identical with compound IV. Hence, $a=b=c$, and the proof of the equality of the three hydrogen atoms is complete.

From the known constitution of mesitylene it is possible to infer the structure of many other compounds. The method is exemplified by its partial oxidation to *mesitylenic acid,*



a substance convertible into xylene by distillation with lime, indicating this xylene to be the *meta*-compound. Oxidation converts *m*-xylene into metaphthalic acid, demonstrating the carboxyl-groups in that acid to occupy the *meta*-position. These determinations of position have been substantiated fully by the application of KÖRNER's principle, NÖLTING having prepared three isomeric nitroxylenes with their methyl-groups situated similarly to those in the xylene obtained from mesitylenic acid.

Among other *meta*-compounds with the position of their groups established independently is a dibromobenzene boiling at 220°. KÖRNER demonstrated the existence of three isomeric tribromobenzenes and three nitrodibromobenzenes corresponding with this substance. In conclusion, the phenylenediamine melting at 62° can be obtained from three different diaminobenzoic acids by elimination of carbon dioxide, indicating it also to be a *meta*-compound.

3. Absolute Determination of Position for *para*-Compounds.

357. KÖRNER's principle has been of great service in determining the constitution of some members of the *para*-series. An example is the possibility of obtaining only one nitroxylene from the xylene boiling at 138°, and melting at 13°. The phenylenediamine melting at 140° can be obtained by elimination of carbon dioxide from one diaminobenzoic acid only; and other instances could be cited.

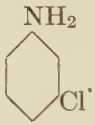
These determinations of position have been confirmed by another method, exemplified by the identification as a *para*-compound of a hydroxybenzoic acid melting at 210°. The starting-point of the proof is bromobenzoic acid, obtained directly by the bromination of benzoic acid. Nitration gives two isomeric nitrobromobenzoic acids, each yielding by reduction the same aminobenzoic acid, anthranilic acid. This acid can be converted into salicylic acid by the diazo-reaction. Consequently, in each isomeride the nitro-group must be situated sym-

metrically to the carboxyl-group; at 2 or 6, or at 3 or 5, assuming the carboxyl-group to be at 1. Similar reasoning establishes the position of the hydroxyl-group in salicylic acid. The bromine atom cannot be at 4, because two isomeric nitro-compounds yielding the same amino-benzoic acid by reduction could not be obtained from

The bromine atom therefore must occupy the *meta*-position or the *ortho*-position to the carboxyl-group. A hydroxybenzoic acid melting at 200°, and corresponding with this bromo-acid must be therefore *meta* or *ortho*. As the isomeric salicylic acid also must be a *meta*-compound or an *ortho*-compound, there remains only the *para*-structure for the third hydroxybenzoic acid melting at 210°.

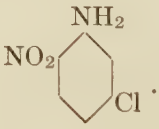
Determination of Position for the Trisubstituted and Higher-substituted Derivatives.

358. Usually, the orientation of trisubstituted and higher-substituted derivatives can be effected by ascertaining the relationship of the compounds to di-derivatives of known constitution. An example is furnished by a certain chloronitroaniline, $C_6H_3Cl(NO_2)(NH_2)$, obtained by nitrating *m*-chloroaniline,

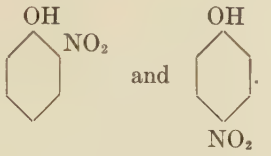


The formation of *p*-chloronitrobenzene,

by exchange of the amino-group for hydrogen indicates it to have the constitutional formula



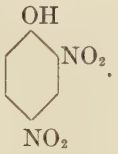
A more complex example of orientation is afforded by the determination of the positions of the groups in *picric acid*. Gentle nitration converts phenol into two mononitrophenols,



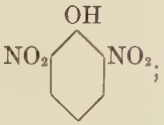
M.P. 45° M.P. 114°

One of these mononitrophenols must be the *ortho*-compound and the other must be the *para*-compound, because the third nitrophenol can be obtained from *m*-dinitrobenzene by reduction to *m*-nitroaniline, and subsequent exchange of the amino-group for hydroxyl by diazotizing. The constitution of *m*-dinitrobenzene follows from its reduction to *m*-phenylenediamine (**339**).

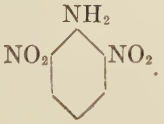
Further nitration of both nitrophenols yields the same dinitrophenol, indicating its formula to be



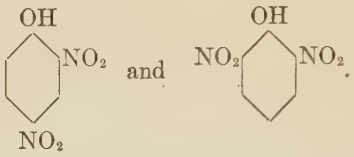
The mononitrophenol melting at 114° is converted by oxidation into benzoquinone (**338**), and therefore must be the *para*-compound. For the substance melting at 45° there remains only the *ortho*-structure. Nitration of this *o*-nitrophenol yields, in addition to 1:2:4-dinitrophenol (OH at 1), another dinitrophenol with its groups at 1:2:6. This derivative has the formula



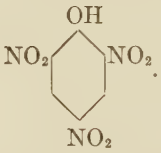
for heating its methyl ether with alcoholic ammonia replaces the methoxyl-group by the amino-group, yielding a substance with the formula



By substitution of hydrogen for the amino-group, this product is converted into the ordinary *m*-dinitrobenzene. There are therefore two dinitrophenols of known structure,



Further nitration converts both into picric acid, and it must have the constitution



From the structural formula of picric acid may be inferred the position of the groups in ordinary trinitrobenzene, this compound being oxidized readily to picric acid (**334**). Accordingly, this trinitrobenzene must have the symmetrical structure.

Equivalence of the Six Hydrogen Atoms in Benzene.

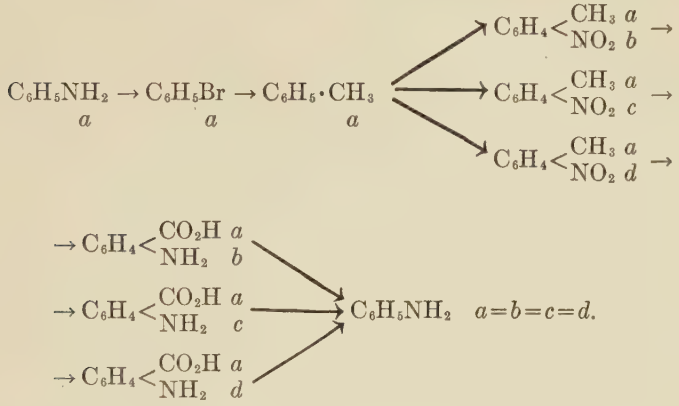
359. Benzene is stated in **286** not to yield isomeric monosubstitution-products, and the six hydrogen atoms of this hydrocarbon are inferred to be of equal value.

There are several direct methods of proving this equivalence, one of them, devised by NÖLTING, being characterized by its simplicity. Denoting the six hydrogen atoms by *a*, *b*, *c*, *d*, *e*, and *f*, the amino-group in aniline may be assumed arbitrarily to be at *a*. Bromobenzene is obtained from aniline by the diazo-reaction (**307**, 4), and reacts with methyl iodide and sodium to yield toluene. Nitration of toluene gives three isomeric nitrotoluenes, the proportion of the *meta*-compound being very small. In these compounds the methyl-group is at *a*, and the nitro-groups may be assumed arbitrarily to be at *b*, *c*, and *d*. Reduction yields the three corresponding toluidines:

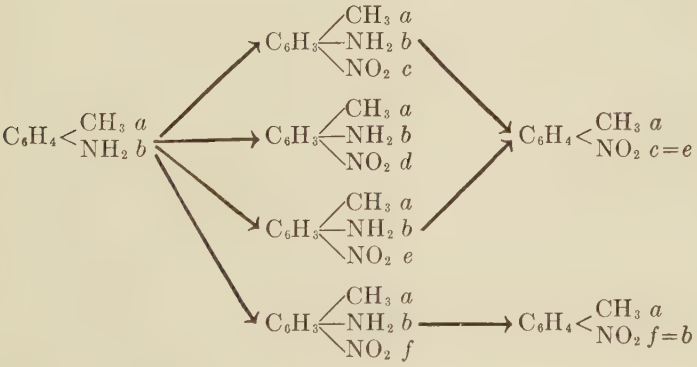
$$C_6H_5\cdot CH_3(a) \rightarrow CH_3\cdot C_6H_4\cdot NO_2(b{:}c{:}d) \rightarrow COOH\cdot C_6H_4\cdot NH_2(b{:}c{:}d).$$

After protection of the amino-group in each of these compounds by acetylation, the three aminobenzoic acids are obtained by oxidation. By elimina-

tion of carbon dioxide, these acids give a derivative identical with the original aniline, indicating $a=b=c=d$:



The starting-point of the proof of the equivalence of e and f to a, b, c, and d is o-toluidine, its methyl-group being assumed to be at a, and the amino-group at b. Nitration of its acetyl-derivative and elimination of the acetyl-group produce simultaneously four nitro-o-toluidines. Positions a and b being occupied, the nitro-groups must be at c, d, e, and f. Replacement of the amino-group by hydrogen yields four nitrotoluenes, $a{:}c$, $a{:}d$, $a{:}e$, and $a{:}f$. The first two are m-nitrotoluene and p-nitrotoluene; they are obtained also by direct nitration of toluene, as described in the previous paragraph. The nitrotoluene $a{:}e$ is identical with $a{:}c$, and $a{:}f$ with $a{:}b$, indicating the equivalence of c to e and of b to f, and completing the proof:



Influence of the Substituents on Each Other.

360. The introduction of a second substituent into a monosubstituted benzene derivative, C_6H_5X, forms the three theoretically possible di-derivatives in very unequal proportion. There are two main types of substitution, either the *para*-derivative and the *ortho*-derivative predominating, or the *meta*-derivative constituting the chief product. The table summarizes the most important types of substitution, the numbers in brackets indicating the by-products, and being arranged in order of diminishing proportion.

Element or Group already Present (in Position 1).	Position Entered by Substituents.				
	Cl	Br	I	SO_3H	NO_2
Cl	4(2)(3)	4(2)(3)	4	4	4(2)
Br	4(2)(3)	4(2)(3)	—	4	4(2)
I	4	4	4	4	4(2)
OH	4(2)	4(2)	4(2)	4(2)	4(2)
SO_3H	—	3	—	3(4)	3(2)(4)
NO_2	3	3	—	3(2)(4)	3(2)(4)
NH_2	4(2)	4	4	4(2)	4(2)
CH_3	4(2)	4(2)	4(2)	4(2)(3)	2(4)(3)
COOH	3	3	3	3(4)	3(2)(4)
CN	—	—	—	—	3
NO	4	4	—	—	4
SCH_3	—	4(2)	—	4(2)	—

The table indicates a second substituent to be directed into the *para*-position and the *ortho*-position by the presence of halogens and the groups hydroxyl, amino, and methyl; but into the *meta*-position by the groups sulpho, nitro, carboxyl, and cyano. In each type the influence is exerted independently of the nature of the substituent introduced. This rule is of general application, and is known as the *rule of the constancy of substitution-type.*

The relative proportions of the isomerides formed vary greatly even for the same type of substitution, and depend on three factors: (1) the substituent already present; (2) the substituent introduced; (3) the experimental conditions. These three factors are powerless to modify the substitution-type, for it is almost invariable; but they cause important changes in the proportions of the isomerides formed in each type. A few examples illustrating this influence are subjoined.

1. Nitration at 0° of fluorobenzene yields 12·4 per cent. of the *ortho*-nitro-product, and 87·6 per cent. of the *para*-nitro-product. Nitration at the same temperature of chlorobenzene produces 30·1 per cent. of *o*-chloronitrobenzene, and 69·9 per cent. of *p*-chloronitrobenzene.

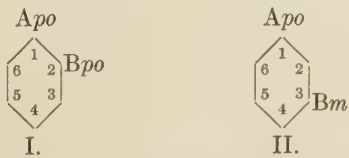
2. The chlorination at 90° of phenol gives 50·2 per cent. of *p*-chlorophenol, and 49·8 per cent. of *o*-chlorophenol. Bromination under the same conditions yields 90·7 per cent. of *p*-bromophenol, and 9·3 per cent. of *o*-bromophenol. These percentages indicate the great influence exerted by the substituent introduced on the proportion of the isomerides formed, even with substituents so similar as chlorine and bromine.

3. Temperature is one of the important factors in the experimental conditions. In nitration-processes it exerts little influence on the proportion of the isomerides. At −30°, nitration of benzoic acid gives 14·4 per cent. of *o*-nitrobenzoic acid, 85·0 per cent. of *m*-nitrobenzoic acid, and 0·6 per cent. of *p*-nitrobenzoic acid; at 30°, the corresponding percentages are 22·3, 76·5, and 1·2. The temperature can exert a very important influence on the course of sulphonation-processes. Sulphonation of toluene at 0° with excess of sulphuric acid gives 53·5 per cent. of *p*-toluenesulphonic acid, 3·8 per cent. of *m*-toluenesulphonic acid, and 42·7 per cent. of *o*-toluenesulphonic acid; for sulphonation at 100° the corresponding percentages are 72·5, 10·1, and 17·4.

In halogenation-processes the nature of the catalyst influences the proportion of the isomerides formed. The chlorination of chlorobenzene with 0·5 per cent. of aluminium chloride as catalyst yields 65·7 per cent. of *p*-dichlorobenzene, 29·6 per cent. of *o*-dichlorobenzene, and 4·7 per cent. of *m*-dichlorobenzene; with an equivalent proportion of ferric chloride as catalyst the corresponding percentages are 55·5, 39·2, and 5·3.

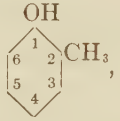
361. The introduction of a third substituent C into a benzene derivative C_6H_4AB raises an interesting problem. Assuming the isomerides formed by the introduction of C into C_6H_5A and into C_6H_5B, and the proportion of each, the problem concerns the possibility of predicting the isomerides C_6H_3ABC formed by the introduction of C into C_6H_4AB, and the proportion of each.

In a qualitative sense prediction is possible, but the problem is much more complex than a superficial consideration indicates. For a benzene derivative C_6H_4AB with formula I,



both A and B directing substitution to the *ortho*-position and the *para*-position, the third substituent would be expected to enter at 4 and 6 under

the influence of A, and at 3 and 5 under the influence of B, the four possible isomerides being formed. Similarly, in combination II, B*m* indicating direction by B of a new substituent to the *meta*-position, A would be expected to direct a new substituent to positions 2, 4, and 6, and B to direct it to position 5. In practice, the relations are much more complex, although there are instances of the formation of the four isomerides, exemplified by *o*-chlorotoluene, corresponding with formula I. In other examples such as that of *o*-cresol,



substitution is at positions 4 and 6 only; but with compounds of type II substitution at position 5 has never been observed.

The explanation must lie in the fact of the velocities of the substitution induced by the substituents already present having very divergent values. Assuming the velocity of substitution due to the hydroxyl-group in *o*-cresol to be one hundred times as great as that due to the methyl-group, the extent of substitution at positions 3 and 5 would be so small as to render detection of the products impossible. In compounds of type II substitution inevitably is much more rapid at the *para*-position and the *ortho*-position than at the *meta*-position.

A study of the different examples of substitution in compounds C_6H_4AB, and a quantitative estimation of the isomerides formed, enable the velocities induced by the various substituents to be arranged in order, although almost invariably the attainment of such an arrangement by direct determination is precluded. The groups causing substitution at the *para*-position and the *ortho*-position exert their influence in the order

$$OH > NH_2 > \text{halogens} > CH_3;$$

and the much less powerful groups causing substitution at the *meta*-position are in the order

$$COOH > SO_3H > NO_2.$$

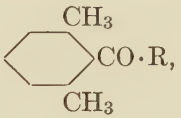
Inversely, knowing these orders of velocity, it is possible to predict the isomerides obtainable in a given reaction. The procedure is exemplified by chlorophenol, the substituent being introduced mainly at the *ortho*-position and the *para*-position to hydroxyl; and by chlorobenzoic acid, replacement occurring chiefly in the *ortho*-position and the *para*-position to chlorine.

362. This opposition between *ortho*-derivatives and *para*-derivatives on the one hand, and *meta*-derivatives on the other, is observed not only in their preparation, but also in many of their properties. As a class, the *meta*-compounds are more stable towards reagents than the *ortho*-derivatives and *para*-derivatives. An example is given in **331**.

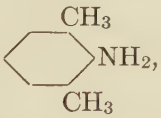
Ortho-groups sometimes exert a remarkable influence in retarding or partially preventing reactions induced readily in their absence. The following reactions exemplify this phenomenon.

Normally, an acid dissolved in excess of absolute alcohol can be converted into an ester almost quantitatively by a current of hydrogen chloride (**93**, 1), but Victor Meyer and his students failed to esterify by this method acids containing two groups in the *ortho*-position relative to carboxyl,

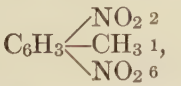
Inversely, the ester formed from such an acid by means of the silver salt and an alkyl halide can be saponified only with difficulty. With the two substituents at any of the other positions, these peculiarities are wholly, or in great measure, lacking. Ketones substituted in the two *ortho*-positions,



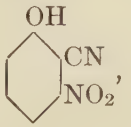
R being an alkyl-radical, cannot be converted into oximes, a distinction from all other ketones. *o*–*o*-Dimethylaniline,



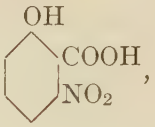
is not converted by an alkyl iodide into a quaternary salt. Pentamethylbenzonitrile, $C_6(CH_3)_5CN$, cannot be hydrolyzed to the corresponding acid. The methyl-hydrogen in *o*–*o*-dinitrotoluene,



cannot be replaced by halogens even at a high temperature (200°), as is true also of 1:2:4-dinitrotoluene. In spite of numerous attempts, the hydrolysis of 3-nitro-2-cyanophenol,

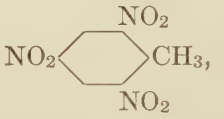


to the corresponding acid,



has not been effected.

Groups occupying positions wider apart sometimes exert a similar effect. One of the nitro-groups of symmetrical trinitrobenzene is replaced by methoxyl through the action of sodium methoxide; but in trinitrotoluene,



analogous substitution has not been possible, the methyl-group preventing exchange of nitro-group 3.

Certain instances of *ortho*-substituents increasing the reactivity of a group situated between them are known.

HYDROCYCLIC OR HYDROAROMATIC COMPOUNDS.

363. There exists a series of natural compounds with proportions of hydrogen intermediate between those in the aromatic derivatives with saturated side-chains and those in the saturated aliphatic derivatives. These *hydrocyclic* or *hydroaromatic* compounds are converted readily into aromatic bodies. They are derivatives of hydrocarbons with the formula C_nH_{2n} having two hydrogen atoms less than the corresponding saturated hydrocarbons, C_nH_{2n+2}, but nevertheless displaying all the properties characteristic of saturated compounds. The explanation is their lack of multiple bonds, and the presence of a closed carbon chain as in *cyclo*hexane,

$$CH_2 < \begin{matrix} CH_2—CH_2 \\ CH_2—CH_2 \end{matrix} > CH_2.$$

The *terpenes*, $C_{10}H_{16}$, are vegetable-products, and are the principal constituents of the "essential oils." These oils also contain compounds of the formulæ $C_{10}H_{16}O$, $C_{10}H_{18}O$, and $C_{10}H_{20}O$, among them the *camphors*. The terpenes and camphors are converted readily into aromatic compounds, and therefore belong to the hydrocyclic series.

Caucasian petroleum consists mainly of cyclic hydrocarbons known as *naphthenes* with the formula C_nH_{2n}. PICTET considers this variety of petroleum to have had its origin in the slow decomposition of resins present in pine and many other types of wood. Normally, this petroleum is optically active, indicating the transformation to have taken place at a relatively low temperature. This hypothesis receives support from the fact that the hydrocarbons of vacuum-tar (283) belong chiefly to the series C_nH_{2n}.

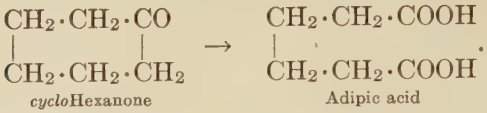
One of the two principal methods employed in the preparation of these hydrocarbons utilizes aliphatic compounds, the other process depending on the use of aromatic derivatives. Several examples of each method will be cited.

The dry distillation of calcium adipate yields *cyclo*pentanone, and that of calcium pimelate gives cyclo*hexanone*:

$$CH_2 < \begin{matrix} CH_2 \cdot CH_2 \cdot COO \\ CH_2 \cdot CH_2 \cdot COO \end{matrix} > Ca = CH_2 < \begin{matrix} CH_2 \cdot CH_2 \\ CH_2 \cdot CH_2 \end{matrix} > CO + CaCO_3.$$

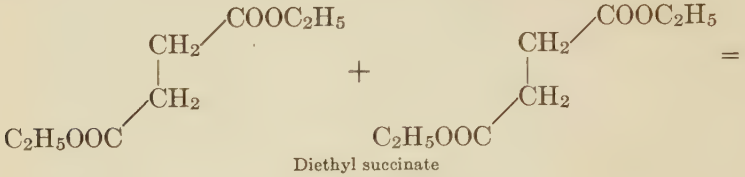
Calcium pimelate — *cyclo*Hexanone

This structural formula is indicated for *cyclo*hexanone by the ketonic character of the compound, and by its almost quantitative oxidation by dilute nitric acid to adipic acid:

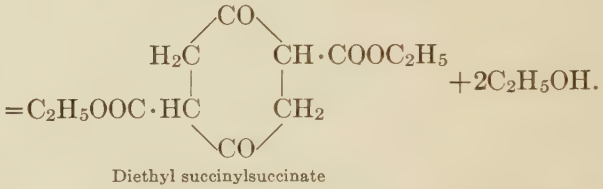


*cyclo*Hexanone — Adipic acid

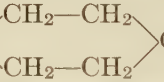
Diethyl succinate constitutes an important basis for the synthesis of other *cyclo*hexane derivatives. In presence of sodium, two molecules of it condense to diethyl succinylsuccinate, an ester melting at 127°:



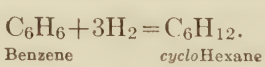
Diethyl succinate



Diethyl succinylsuccinate

The free acid is obtained by saponification, and decomposes at 200° with elimination of two molecules of carbon dioxide, yielding p-*diketo*cyclo*hexane*,  . The structural formula of this substance is indicated by this synthesis, and also by its reduction to *cyclo*hexanone.

The second method of obtaining hydrocyclic compounds depends on the reduction of aromatic derivatives. The procedure devised by Sabatier and Senderens involves passing a mixture of the vapour and hydrogen over finely-divided nickel at temperatures between 150° and 200°. In Willstätter's process, hydrogen at the ordinary temperature is passed through the undiluted liquid compound, or through its solution in ether or glacial acetic acid, platinum-black formed by reduction of a solution of platinum chloride with formaldehyde and sodium hydroxide being employed as catalyst:



Benzene — *cyclo*Hexane

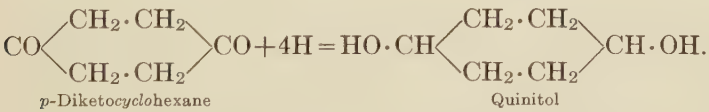
In describing the hydrocyclic compounds, it is convenient to consider separately the cymene derivatives or terpenes, for they exhibit many characteristic properties. The other hydrocyclic compounds will be reviewed briefly first.

364. cyclo*Hexane* is the simplest member of this group. The best method for its preparation is the hydrogenation of benzene by the method of SABATIER and SENDERENS. Like its homologues, it is a colourless liquid. Its boiling-point, 80°, is very near to that of benzene, 80·4°. The isolation of this hydrocarbon from the crude hydrogenation-product of benzene by fractional distillation is therefore impracticable. In its separation, advantage is taken of its stability towards fuming sulphuric acid or concentrated nitric acid at the ordinary temperature, the first converting the benzene present in the crude product into benzene-sulphonic acid and the second into nitrobenzene. Each of these compounds being soluble in the corresponding acid, and *cyclo*hexane insoluble, the separation of the hydrocarbon can be effected readily. The melting-point (82) affords the best criterion of the purity of *cyclo*hexane. It is 6·4°, approximating closely to that of benzene, 5·4°.

In diffused sunlight chlorine reacts very energetically with *cyclo*hexane, and in direct sunlight with explosive violence. A mixture of substitution-products is formed, and yields *monochloro*cyclo*hexane* by fractional distillation. Replacement of the chlorine atom in this compound by hydroxyl is not effected readily; but alcoholic potassium hydroxide converts it into cyclo*hexene*, a liquid boiling at 83°–84°, and possessing all the properties characteristic of unsaturated compounds.

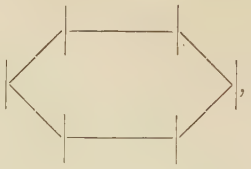
When a mixture of phenol-vapour and hydrogen is passed over finely-divided nickel, cyclo*hexanol* is formed. It is a colourless and somewhat viscid liquid boiling at 160·5°. At a low temperature it solidifies to a camphor-like mass melting at 20°.

p-*Diketo*cyclo*hexane* (**363**) melts at 78°. Gentle reduction with sodium-amalgam in an atmosphere of carbon dioxide converts it into the dihydric alcohol *quinitol*:

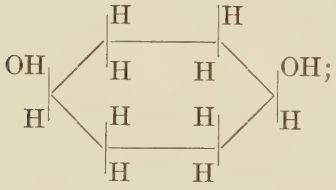


p-Diketo*cyclo*hexane Quinitol

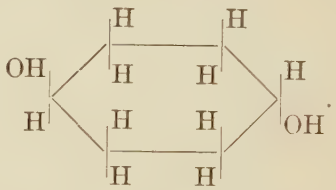
Two modifications of quinitol are known, distinguished by the prefixes *cis* and *trans*. They are prepared best from quinol by the reduction-method of SABATIER and SENDERENS (**363**). They can be separated by means of their acetyl-derivatives. The stereochemical character of their isomerism is indicated by a consideration of Fig. 31 (**167**) representing a *cyclo*pentyl-ring. Assuming the pentagon to lie in the plane of the paper, one of the free bonds of each carbon atom will lie above that plane, and the other below it. Similar construction of a *cyclo*hexyl-ring gives the perspective figure



the affinities not forming part of the ring being represented by vertical lines. The isomerism of the quinitols is explained by assuming the hydroxyl-groups of the *cis*-modification to be situated on the same side of the hexagon, and those of the *trans*-modification to be on the opposite side:

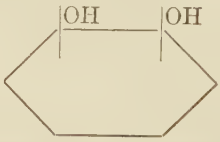


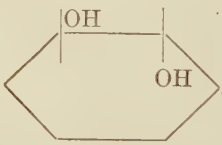
cis-Quinitol (M.P. 101°)



trans-Quinitol (M.P. 139°)

Two isomerides are possible also for *cyclo*hexanediol-1:2, and can be represented by the figures



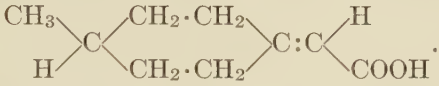


As a sequel to the facts cited in 337 the *cis*-form would be expected to show a great increase in conductivity on addition of boric acid, but the *trans*-form would not; and similar behaviour would be anticipated for the *cis*-form and the *trans*-form of *cyclo*heptanediol-1:2. Whilst experiment has demonstrated the positive effect to be lacking for *cis-cyclo*hexanediol-1:2, it has indicated both the *cis*-form and the *trans*-form of *cyclo*heptanediol-1:2 to be capable of increasing the conductivity of boric acid. The positions of the hydroxyl-groups in *cis-cyclo*hexanediol-1:2 must therefore be assumed to be unfavourable to the production of this effect, whereas those occupied by the hydroxyl-groups in the *cis*-form and the *trans*-form of *cyclo*heptanediol-1:2 must be regarded as favourable.

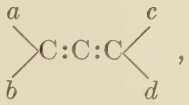
Böeseken made these experiments, and considered the phenomena to be associated with the presence of undulating, and not of plane, rings (280). If this view be correct, the behaviour of the two hydroxyl-groups of *cis-cyclo*hexanediol-1:2 would be governed by their mutual repulsion, as with glycol, and the substance would be unable to combine with boric acid. On the other hand, the great mobility of a *cyclo*heptane-ring would bring the two hydroxyl-groups of *trans-cyclo*heptanediol-1:2 into positions favourable to union with boric acid, thereby forming a five-membered ring.

Inositol, $C_6H_{12}O_6$, is a hexahydric alcohol derived from *cyclo*hexane, and has a molecular formula similar to that of the hexoses. On account of its sweet taste and its occurrence in many leguminous plants, it was classed formerly with the carbohydrates. Its relationship to *cyclo*hexane is indicated by its reduction with hydrogen iodide to benzene, phenol, and tri-iodophenol, and by its conversion through phosphorus pentachloride into quinone and substituted quinones. The presence of six hydroxyl-groups is demonstrated by the formation of a hexa-acetate. Inositol is also a constituent of the heart-muscle, the liver, and the brain.

An important derivative of *cyclo*hexane is 1-*methyl*cyclo*hexylidene*-4-*acetic acid,*

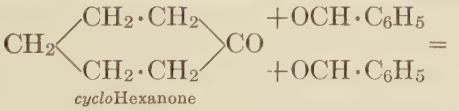


This substance affords a striking example of optical activity occasioned by "Dissymétrie moléculaire" (**196**), for it lacks an asymmetric carbon atom, and yet can be resolved into its optically antipodes. It is one of the substances of the type

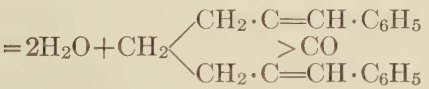


one of the double bonds being replaced by a ring of six carbon atoms. The mirror-images of such substances cannot be superimposed, and in the year 1874 VAN 'T HOFF predicted the discovery of their optical activity.

cyclo*Hexanone* can be prepared from pimelic acid (**363**), but is obtained more readily by the oxidation of *cyclo*hexanol with chromic acid. It boils at 155°. Its alkaline solution reacts with benzaldehyde to form the well-crystallized condensation-product *dibenzal*cyclo*hexanone*:



*cyclo*Hexanone



Dibenzal*cyclo*hexanone

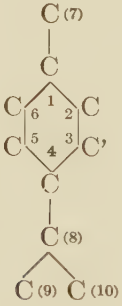
This reaction furnishes a good test for *cyclo*hexanone.

The properties of the hydrocyclic acids are analogous to those of the aliphatic acids, *hexahydrobenzoic acid* having a rancid odour like that of capric acid. It melts at 92°, almost 30° lower than benzoic acid, a substance melting at 121·4°. The hydrophthalic acids exhibit isomerism explicable like that of quinitol.

TERPENES.

365. The *terpenes* are hydrogenated derivatives of cymene and its substitution-products. Many of them are vegetable products. They volatilize readily with steam, and this property facilitates the isolation of the natural terpenes. The distillate separates into two parts, an aqueous layer below, and a mixture of terpenes above. The dried terpene-layer is fractionated several times *in vacuo* to isolate its constituents. Sometimes complete purification of the terpenes has to be effected by their conversion into derivatives separable from impurities by crystallization, it being possible to regenerate the terpenes from the crystalline compounds obtained.

VON BAEYER devised a rational nomenclature for the numerous derivatives of hydrogenated cymene. He numbered the carbon atoms of this hydrocarbon as in the scheme



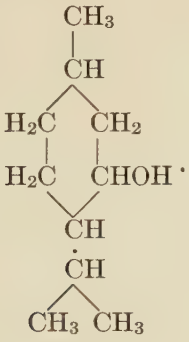
a double bond between two carbon atoms such as 3 and 4 being denoted by Δ^3.

The saturated cyclic hydrocarbon *hexahydrocymene*, $C_{10}H_{20}$, is termed *menthane*. It is not a natural product, but can be obtained by the interaction of cymene and hydrogen with nickel as a catalyst. It boils at 168°.

The saturated alcohols and ketones derivable from menthane are very important. Among them is *menthol* or 3-*menthanol*, $C_{10}H_{20}O$, the principal constituent of oil of peppermint. It crystallizes from

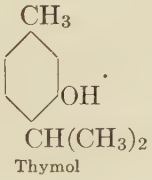
that oil on cooling, and forms colourless prisms of characteristic peppermint-like odour. It melts at 43°.

Menthol has the constitution



Menthol

It is a secondary alcohol, oxidation with chromic acid eliminating two atoms of hydrogen to form a substance of ketonic character termed *menthone*, a constituent of oil of peppermint. As there are several processes for the conversion of menthol into cymene or its derivatives, it must contain a cymene-residue. One of these methods also proves the hydroxyl-group to be attached to carbon atom 3. It involves the action of bromine on a solution of menthone in chloroform, the product being a *dibromomenthone*. Quinoline eliminates two molecules of hydrogen bromide from each molecule of this substance, forming thymol (294),



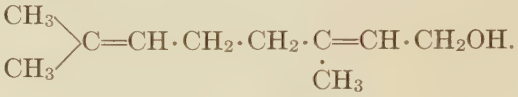
Thymol

Heating thymol with phosphoric oxide yields propene and *m*-cresol (294), indicating its methyl-group and hydroxyl-group to be at the *meta*-position.

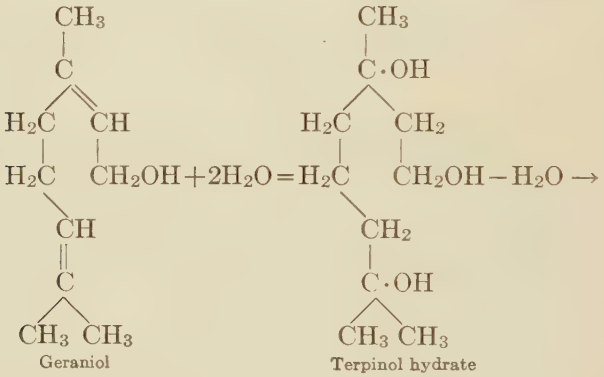
366. *Terpinol*, $C_{10}H_{18}(OH)_2$, is a dihydric alcohol theoretically derived from menthane. Its *hydrate*, $C_{10}H_{20}O_2,H_2O$, is obtained by keeping oil of turpentine in contact with dilute nitric acid and a small proportion of alcohol in shallow dishes for several days. During the process the turpentine combines with the elements of three molecules of water. Terpinol hydrate forms well-defined crystals melting at 117°.

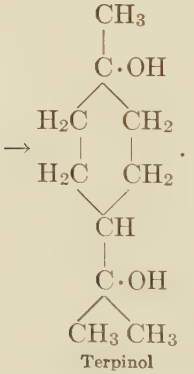
From each molecule heat expels one molecule of water, anhydrous terpinol distilling at 258°.

Terpinol can be synthesized from geraniol,



Prolonged agitation with sulphuric acid of five per cent. strength causes each molecule of geraniol to combine with two molecules of water, and become converted almost quantitatively into terpinol hydrate:





This mode of synthesis indicates terpinol to be 1:8-dihydroxymenthane, and there is other evidence in favour of this view. Hydrogen iodide reduces it to menthane, proving the presence of a cymene-nucleus.

The constitutional formula given for terpinol is confirmed by the synthesis of this compound effected by W. H. Perkin, Jun. Ethyl

sodiocyanoacetate and ethyl 2-iodopropionate react in accordance with the equation

$$2CN\cdot CHNa\cdot COOC_2H_5+2I\cdot CH_2\cdot CH_2\cdot COOC_2H_5=2NaI+$$

$$+\begin{matrix} & CN & & CH_2\cdot CH_2\cdot COOC_2H_5 \\ C_2H_5OOC & & C & \\ & & & CH_2\cdot CH_2\cdot COOC_2H_5 \end{matrix}+CN\cdot CH_2\cdot COOC_2H_5.$$

I.

Hydrolysis of compound I simultaneously eliminates carbon dioxide, with formation of the acid

$$HOOC\cdot CH\begin{matrix} CH_2\cdot CH_2\cdot COOH \\ CH_2\cdot CH_2\cdot COOH \end{matrix}.$$

From it water and carbon dioxide are removed by heating with acetic anhydride, the ketonic acid

$$HOOC\cdot CH\begin{matrix} CH_2\cdot CH_2 \\ CH_2\cdot CH_2 \end{matrix}CO$$

being formed. The carbethoxyl-group and the carbonyl-group of the ester of this acid react readily with methyl magnesium iodide (**91** and **102**), giving a compound of the formula

$$\begin{matrix} CH_3 \\ CH_3 \\ I\cdot MgO \end{matrix}C\cdot CH\begin{matrix} CH_2\cdot CH_2 \\ CH_2\cdot CH_2 \end{matrix}C\begin{matrix} OMg\cdot I \\ CH_3 \end{matrix},$$

converted by dilute mineral acids into the product

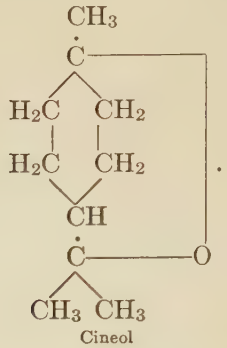
$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}C\cdot CH\begin{matrix} CH_2\cdot CH_2 \\ CH_2\cdot CH_2 \end{matrix}C\begin{matrix} OH \\ CH_3 \end{matrix},$$

$$\dot{O}H$$

identical with terpinol.

Elimination of water from terpinol yields, among other products (**367**), a substance of the formula $C_{10}H_{18}O$. It is neither an alcohol nor a ketone, and is identical with *cineol*, a constituent of many essential oils. Oil of eucalyptus and oil of wormseed (*Oleum cinæ*) contain a

large proportion of this compound. Its mode of formation and properties indicate cineol to have the constitutional formula

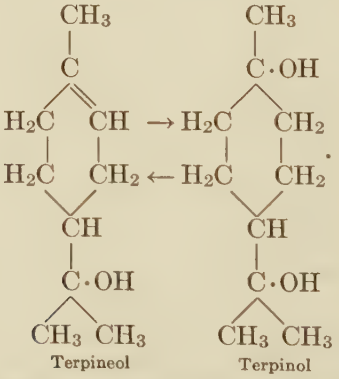


Cineol

367. Some of the unsaturated derivatives of menthane are also very important. The *menthenes*, $C_{10}H_{18}$, hydrocarbons with one double bond in their molecule, need not be considered; but the alcohol *terpineol* and the ketone *pulegone*, derived from them, merit description.

Terpineol, $C_{10}H_{18}O$, is a constituent of some essential oils. It has an odour resembling that of lilacs, melts at 35°, and boils at 218°. Terpineol is related closely to terpinol, agitation with dilute sulphuric acid converting it into terpinol hydrate. Inversely, boiling with dilute sulphuric acid regenerates terpineol from terpinol hydrate, with elimination of water.

The constitution of terpineol therefore must be very similar to that of terpinol, the only problem being the identity of the hydroxyl-group eliminated from the molecule of terpinol along with one hydrogen atom. The existence of an optically active terpineol proves it to be the hydroxyl-group at 1, and terpineol to have the constitution indicated in the scheme

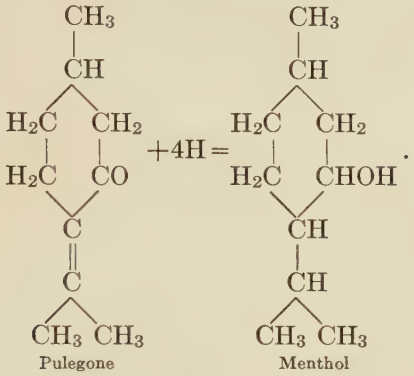


Terpineol Terpinol

Carbon atom 4 in the formula given is asymmetric, but removal of the

elements of water from carbon atoms 4:8, 8:9 (=8:10), or 1:7 could not produce an asymmetric carbon atom.

Pulegone, $C_{10}H_{16}O$, is the principal constituent of the cheap oil of polei (*Mentha pulegium*). It boils at 222°, and has a peppermint-like odour. The formation of an oxime indicates it to be a ketone. Reduction with sodium and alcohol adds four hydrogen atoms to form menthol, proving the carbonyl-group to be at position 3:

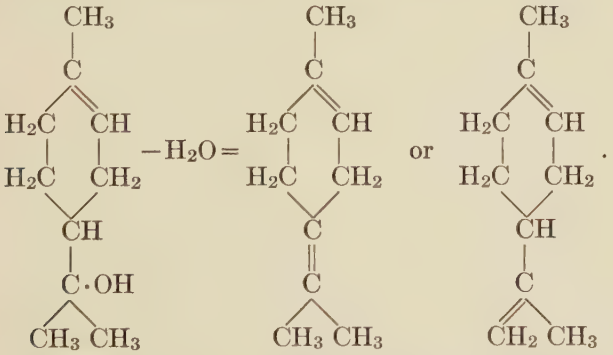


Pulegone Menthol

Both oxidation and heating with water decompose pulegone with formation of acetone, indicating the double bond to be between carbon atoms 4 and 8.

Among the unsaturated menthane derivatives with two double bonds are the hydrocarbons *terpinolene*, d-*limonene*, and l-*limonene*, and racemic limonene or *dipentene*. Each has the formula $C_{10}H_{16}$.

Terpinolene boils at 185°, and is formed by boiling terpineol with oxalic-acid solution, one molecule of water being eliminated. Theoretically, two reactions are possible:

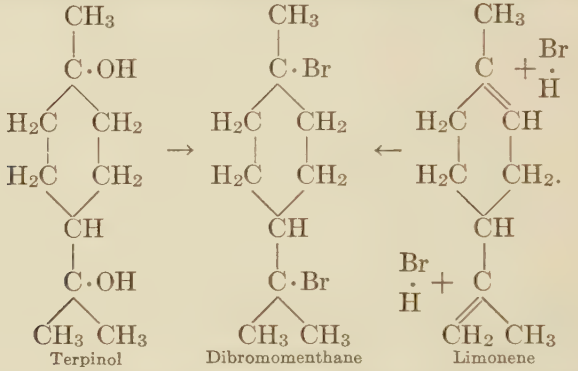


Terpineol I. Terpinolene II. *d*- and *l*- Limonene III.

Terpinolene being optically inactive, and being derived from the opti-

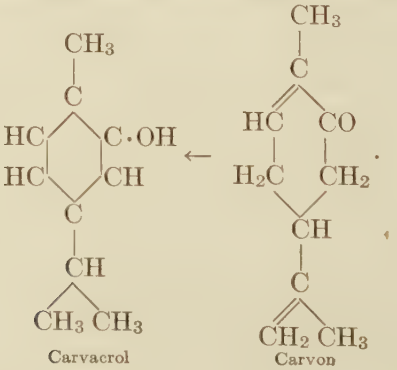
cally active terpineol, the asymmetry of the carbon atom must have vanished, as in formula II. Carbon atom 4 of formula III is asymmetric, as in terpineol itself with formula I.

Formula III is that of the optically active limonene, a constituent of many essential oils and varieties of turpentine. It has an agreeable lemon-like odour. Its constitution is inferred from its production from terpineol by elimination of water, effected by heating with potassium hydrogen sulphate; and from the formation by the addition of two molecules of hydrogen bromide of the same dibromomenthane as is obtained from terpinol by exchange of the hydroxyl-groups for bromine:



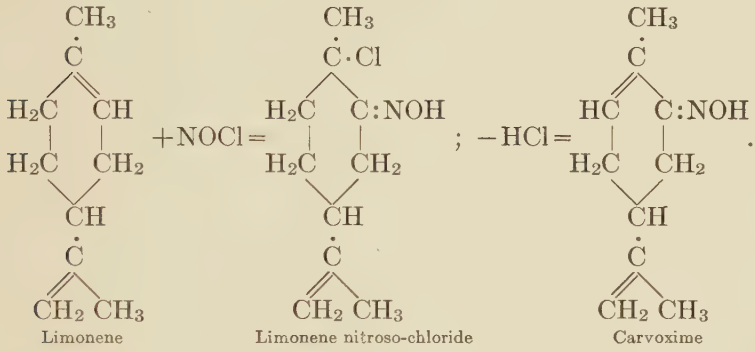
Dipentene, a constituent of oil of turpentine, is formed by mixing *d*-limonene and *l*-limonene in equal proportions by weight. Like the limonenes, it yields a well-crystallized tetrabromide, indicating the presence in its molecule of two double bonds. Isoprene (**127**) can be prepared from limonene by passing its vapour over an electrically-heated platinum spiral.

368. *Carvone*, $C_{10}H_{14}O$, is an important ketone belonging to this group. It is the principal constituent of oil of caraway, and has its characteristic odour. It boils at 228°. Related to carvone is *carvacrol*, obtained from it by heating with potassium-hydroxide solution:



The hydroxyl-group in carvacrol is in union with carbon atom 2, for heating with phosphoric oxide evolves propylene and forms *o*-cresol (294). The carbonyl-group in carvone is assumed therefore to be at position 2. Carvone is proved to be a ketone by the formation of the oxime *carvoxime*.

The addition of nitrosyl chloride to limonene, followed by the elimination from each molecule of one molecule of hydrogen chloride, yields carvoxime:

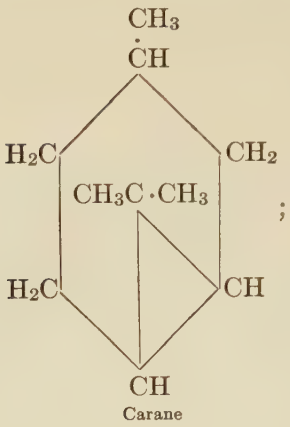


Limonene — Limonene nitroso-chloride — Carvoxime

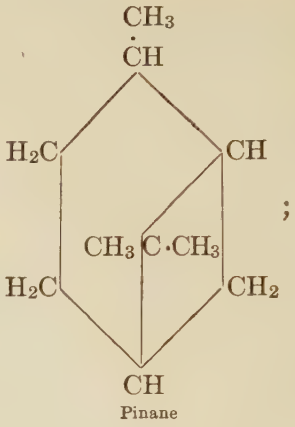
This reaction indicates carvone to contain one double bond $\Delta^{8:9}$, and the other double bond to be Δ^{6} or $\Delta^{1:7}$. In the production of terpineol from terpinol the double bond is formed between two carbon atoms of the nucleus, and by analogy this arrangement should hold for carvone. Further evidence in favour of the formula indicated is afforded by the decomposition-products of the carvone molecule, but the details are beyond the scope of this work.

Polycyclic Terpene Derivatives.

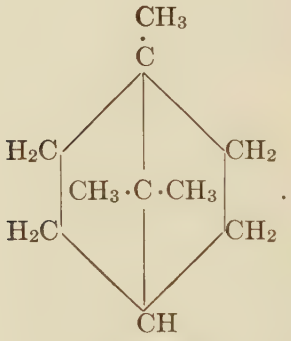
369. There exist hydrocarbons of the formula $C_{10}H_{16}$ with a single double bond, for they add only two univalent atoms or groups. As they contain four hydrogen atoms less than the saturated cyclic menthane, $C_{10}H_{20}$, they must have a second closed chain in the molecule. Moreover, these compounds and their derivatives are related closely to cymene, most of them being convertible into it or into kindred substances. Investigation has revealed the existence of the possibility for the formation of the second ring of the three different modes represented in the formulæ:



Carane



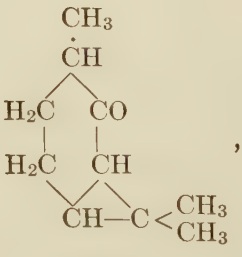
Pinane



Camphane

The tertiary carbon atom takes part in the formation of the ring, or "bridge-formation." *Carane* has a trimethylene-ring, *pinane* a tetramethylene-ring, and *camphane* a pentamethylene-ring. Several members of these three groups will be considered.

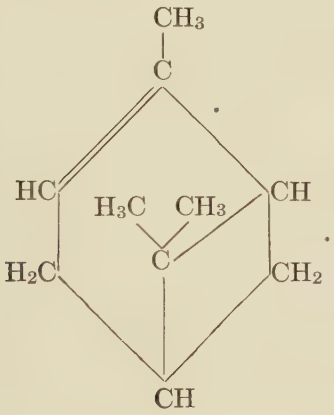
Carane is a liquid boiling at 169°, and is obtained by the reduction of *carone*,



Carone

The opening of the trimethylene-ring at 3:8 yields derivatives of *p*-cymene, and at 4:8 derivatives of *m*-cymene.

Pinene is the typical member of the pinane-group. As the principal constituent of the various oils of turpentine, it is of technical importance. It is optically active, a dextrorotatory form, a lævorotatory variety, and an inactive modification being known. It boils at 156°. The presence of a double bond is identified by the addition of an equimolecular proportion of dry hydrogen chloride, the gas precipitating from cooled oil of turpentine a compound of the formula $C_{10}H_{16}$,HCl, termed " artificial camphor," and resembling camphor both in appearance and odour. Pinene also forms readily an addition-product with nitrosyl chloride. Pinene has the formula



The presence of a tetramethylene-ring is assumed to explain the constitution of pinene oxidation-products such as *pinonic acid* and *pinic acid*, and for other reasons. Under the influence of benzenesulphonic acid, pinene in acetic-acid solution combines with one molecule of water to form terpineol, the tetramethylene-ring being opened. This transformation indicates the position of the double bond.

CAMPHORS.

370. Ordinary *camphor*, $C_{10}H_{16}O$, is the most important member of the camphane-group. Ordinary dextrorotatory " Japan camphor " is obtained by the steam-distillation of the bark of the camphor-tree. It forms a white, soft, crystalline mass of characteristic odour, and sublimes even at the ordinary temperature. It melts at 175·7°, and boils at 209·1°.

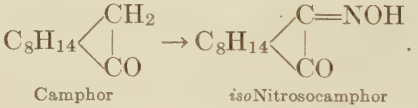
The camphor-odour is characteristic of many compounds having all the hydrogen atoms attached to a single carbon atom replaced. Very few of the relations between odour and chemical constitution have been discovered. Compounds of widely divergent chemical structure often have a very similar odour, as with artificial musk and natural musk. Other substances closely related chemically exhibit complete dissimilarity in smell. This phenomenon is exemplified by the chlorophenols, the *ortho*-compound in the very dilute state having a powerful odour like that of iodoform; but the smell of the *meta*-compound and that of the *para*-compound are much less pronounced, and resemble that of unsubstituted phenol.

Normally, the intensity of odour is greater for unsaturated substances than for the corresponding saturated derivatives. It usually increases with rise in molecular weight in a homologous series until a maximum is attained.

Camphor is a saturated ketone, because it does not yield addition-products, and forms an oxime. Reduction converts it into the secondary alcohol *borneol* or "Borneo camphor":

$$\underset{\text{Camphor}}{C_9H_{16}\cdot CO} + 2H = \underset{\text{Borneol}}{C_9H_{16}\cdot CHOH}.$$

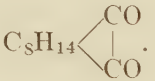
In addition to the carbonyl-group, the camphor molecule contains a methylene-group, for it has the properties of compounds with the group—$CH_2\cdot CO$—. As explained in **199**, the hydrogen of such a methylene-group can be replaced by the oxime-group through the action of amyl nitrite and hydrogen chloride. Camphor reacts similarly, these reagents converting it into iso*nitrosocamphor*, melting at 153°:



$$\underset{\text{Camphor}}{C_8H_{14}\left\langle\begin{matrix}CH_2\\ |\\ CO\end{matrix}\right.} \rightarrow \underset{\textit{iso}\text{Nitrosocamphor}}{C_8H_{14}\left\langle\begin{matrix}C{=}NOH\\ |\\ CO\end{matrix}\right.}.$$

Elimination of the oxime-group from *iso*nitrosocamphor yields *camphor-quinone*,

$$C_8H_{14}\left\langle\begin{matrix}CO\\ |\\ CO\end{matrix}\right..$$



Hydrogen peroxide oxidizes this compound to the anhydride of *camphoric acid*,

$$C_8H_{14}<\begin{matrix}COOH\\ COOH\end{matrix}.$$

It can be obtained also directly from camphor by oxidation with nitric acid. Obviously, a knowledge of the constitution of camphoric acid would enable that of camphor to be inferred.

Ordinary camphoric acid is dextrorotatory, and melts at 187°. The four optically active camphoric acids are dextrorotatory and lævorotatory camphoric acid, and dextrorotatory and lævorotatory iso*camphoric acid* with the same constitution as camphoric acid. These facts indicate the molecule of camphoric acid to contain two dissimilar asymmetric carbon atoms (188).

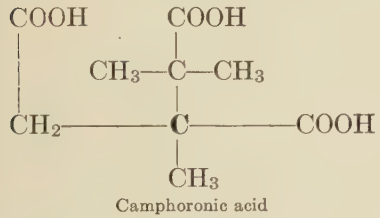
Energetic oxidation converts camphoric acid into the tribasic optically active *camphoronic acid*, its constitution being inferred from its synthesis, and from the decomposition-products formed by its dry distillation. That process decomposes it into trimethylsuccinic acid, *iso*butyric acid, carbon dioxide, and carbon:

$$\begin{array}{l}(CH_3)_2C\cdot COOH\\ \quad\quad|\\ CH_3\cdot C\cdot COOH\\ \quad\quad|\\ \quad CH_2\cdot COOH\end{array}\quad=\quad\begin{array}{l}(CH_3)_2C\cdot COOH\\ \quad\quad|\\ CH_3\cdot CH\cdot COOH\end{array}+C+H_2+CO_2;$$

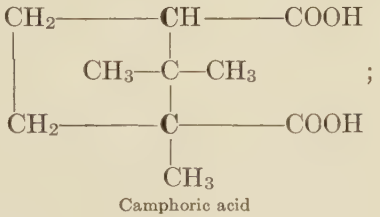
Camphoronic acid

and $$(CH_3)_2CH\cdot COOH+\begin{matrix}CH_3\\CH_3\end{matrix}>CH\cdot COOH+CO_2.$$

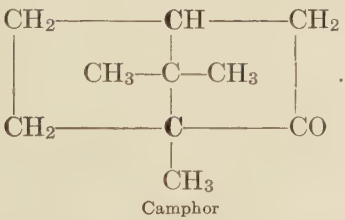
These facts facilitate deduction for camphoric acid of a formula according also with its other properties:



Camphoronic acid



Camphoric acid

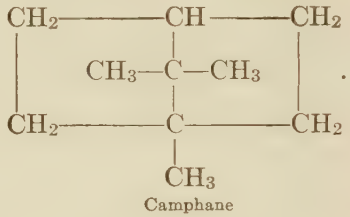


Camphor

This structural formula for camphor was proposed originally by Bredt. His view was confirmed by the synthesis of camphor, effected by W. H. Perkin, jun. and J. F. Thorpe, and also by Komppa, but the details of the processes involved are beyond the scope of this work. The formula of camphor contains two dissimilar asymmetric carbon atoms, represented in bold-face type.

The position of the carbonyl-group in camphor is indicated by its conversion into carvacrol by the action of iodine, the hydroxyl-group in that compound being in the *ortho*-position to the methyl-group (368).

Borneol contains a CHOH-group instead of the carbonyl-group present in camphor. By replacement of the hydroxyl-group by iodine, it yields bornyl iodide, reducible to camphane:



Camphane

According to the formula, the conversion of carbonyl, CO, into methylene, CH_2, should destroy the asymmetry of both the asymmetric carbon atoms of camphor, and camphane is optically inactive.

The formula of camphor contains an *iso*propyl-group and therefore accords with the conversion of camphor into cymene by heating with phosphorus pentasulphide. The complete synthesis of camphoric acid previously mentioned has settled definitely the constitution of this acid, and that of camphor itself.

Camphor finds technical application in the manufacture of "Celluloid," a solid solution of nitrocellulose and camphor of very plastic nature. To render this process independent of the Japanese production of camphor, various methods of synthesizing camphor from turpentine have been devised. One of them involves the addition of hydrogen chloride to pinene, a simultaneous intramolecular rearrangement yielding bornyl chloride. On heating this substance with sodium formate, the chlorine is replaced by the H·COO-group, yielding the formate of *iso*borneol, $C_{10}H_{15}\cdot OH$, a derivative convertible by oxidation into camphor.

POLYTERPENES.

The *polyterpenes* include a number of compounds of the formula $(C_5H_8)_n$, n being greater than 2.

The most important member of the class is *caoutchouc* or *india-rubber*, obtained from *latex*, a fluid present in the laticiferous system of various tropical plants, chief among them being *Hevea brasiliensis*. Incisions are made in the stem of this tree, the process being known technically as "Tapping," and the liberated latex is collected in small tin or earthenware cups. The milk-like fluid is coagulated by the action of a small proportion of acetic acid, the coagulum being passed through

rollers to convert it into sheets. Caoutchouc is purified by dissolving in it chloroform or another solvent, and precipitating it with alcohol in a white amorphous form. It is *vulcanized* by the action of sulphur or sulphur monochloride, S_2Cl_2, a process considerably augmenting its elasticity and durability. Unvulcanized caoutchouc becomes sticky at 30°, and loses its elasticity at 0°. Over-vulcanization yields *ebonite* or *vulcanite*.

PEACHEY'S cold vulcanization process consists in exposing the raw india-rubber to the action of sulphur dioxide and hydrogen sulphide alternately, an active form of sulphur being liberated and the india-rubber vulcanized without the application of heat. The method is much more rapid than the older process, and avoids the cost of steam. It has the additional advantage of enabling many colouring matters destroyed by the usual operation of vulcanization to be employed. Other processes for direct vulcanization of latex have been devised also.

Ozonized air reacts with a solution of caoutchouc in chloroform to produce an ozonide in the form of a vitreous mass. This substance has the empirical formula $C_5H_8O_3$, but its molecular weight must be much higher than that indicated by this formula. The ozonide is converted quantitatively by water into *lævulaldehyde*,

$$CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot C\overset{H}{\underset{O}{}},$$

and a peroxide of that substance.

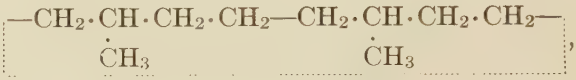
The hydrogenation of caoutchouc with hydrogen at 100° and a pressure of sixty atmospheres in presence of platinum as a catalyst yields a compound of the formula $(C_5H_{10})_x$, and with all the properties of a saturated hydrocarbon. Its nature is exemplified by its stability towards cold, concentrated nitric acid; as well as by the inability of bromine to react with it by addition, only substitution being possible. As an initial product this *hydrocaoutchouc* is amorphous, and has a high molecular weight. Heat decomposes it, the derivative with the lowest molecular weight obtained being 2-*methylbutene*-1 or as-*methylethylethene*,

$$CH_3 \cdot CH_2 \cdot \underset{\displaystyle CH_3}{\overset{\displaystyle \cdot}{C}}{=}CH_2 \quad ;$$

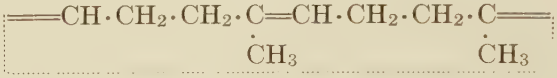
whilst the decomposition of caoutchouc itself under the influence of heat gives 2-*methylbutadiene*-1:3 or isoprene (**127**),

$$CH_2{=}CH \cdot \underset{\displaystyle CH_3}{\overset{\displaystyle \cdot}{C}}{=}CH_2 \,.$$

As its formula is $(C_5H_{10})_x$, hydrocaoutchouc must have a saturated carbon ring. Since the formation of 2-methylbutene indicates the presence in the ring system of a series of such groups, hydrocaoutchouc can be represented by the formula



and caoutchouc itself by



with carbon rings of unknown size. This formula for caoutchouc accounts for the formation of 4-*ketopentanal* by fission at the double bonds, and of isoprene by rupture at the positions next to the double bonds.

The great technical importance of caoutchouc has led in recent years to many attempts to prepare it synthetically. Although polymerization of isoprene (**127**) readily yields a product capable of undergoing vulcanization and characterized by a great resemblance to caoutchouc, the synthetic derivative lacks the fundamental properties constituting the basis of the great practical importance of natural caoutchouc. Despite numerous attempts, and the possibility of preparing isoprene on the large scale, no technically applicable method for the production of caoutchouc has been discovered hitherto.

BENZENE-NUCLEI IN DIRECT UNION, OR INDIRECTLY UNITED BY CARBON.

371. The simplest possible compound of this nature is one containing two benzene-nuclei directly united. In addition, there are compounds with the benzene-nuclei indirectly connected by a carbon atom, or by a chain of carbon atoms. A few typical examples will be cited.

Diphenyl, $C_6H_5 \cdot C_6H_5$.

Diphenyl can be prepared by heating iodobenzene with finely-divided copper at 220°. A better procedure is to pass benzene-vapour through a red-hot iron tube:

$$2C_6H_6 = C_{12}H_{10} + H_2.$$

Another method for the preparation of the derivatives of diphenyl, the conversion of hydrazobenzene into benzidine, is mentioned in **301**. The removal of the amino-groups from benzidine by the diazo-reaction gives diphenyl. This method of formation also affords a proof of the constitution of benzidine.

Oxidation converts diphenyl into benzoic acid. This reaction and the synthesis of diphenyl indicate its constitution.

Diphenyl forms large, tabular, colourless crystals readily soluble in alcohol and ether. It melts at 71°, and boils at 254°.

The isomeric substitution-products of diphenyl are much more numerous than those of benzene, as the scheme indicates:

Diphenyl

A monosubstitution-product can exist in three isomeric forms, the substituent being at the *ortho*-position, the *meta*-position, or the *para*-position to the bond between the benzene-nuclei. In a disubstitution-product both substituents may be attached to the same benzene-nucleus, or to different benzene-nuclei, and so on.

Benzidine is of technical importance, many of the azo-dyestuffs being derived from it.

Diphenylmethane, $C_6H_5 \cdot CH_2 \cdot C_6H_5$.

372. *Diphenylmethane* can be obtained from benzyl chloride $C_6H_5 \cdot CH_2Cl$, or from methylene chloride, CH_2Cl_2, by means of benzene and aluminium chloride. Its homologues are produced by the action of benzene and concentrated sulphuric acid on aldehydes, acetaldehyde yielding *unsymmetrical diphenylethane*:

$$CH_3 \cdot CH \boxed{O + \begin{matrix} H \\ H \end{matrix}} \begin{matrix} C_6H_5 \\ C_6H_5 \end{matrix} = CH_3 \cdot CH < \begin{matrix} C_6H_5 \\ C_6H_5 \end{matrix} + H_2O.$$

Replacement of derivatives of benzene by related compounds enables many derivatives of diphenylmethane to be obtained by this mode of synthesis.

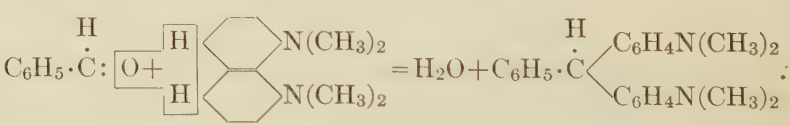
Diphenylmethane is crystalline. It melts at 26°, boils at 262°, and has an odour resembling that of orange-peel. Oxidation with chromic acid converts it into benzophenone (316). Benzilic acid is mentioned in 376.

Triphenylmethane and its Derivatives.

373. *Triphenylmethane*, $CH(C_6H_5)_3$, is formed from benzal chloride $C_6H_5 \cdot CHCl_2$, by the action of benzene and aluminium chloride; from benzaldehyde and benzene in presence of a dehydrator such as zinc chloride; and from the interaction of chloroform and benzene in presence of aluminium chloride. It crystallizes in beautiful colourless prisms melting at 93°. Its boiling-point is 359°.

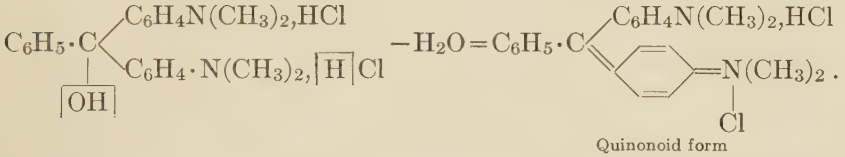
A series of important dyestuffs, the *rosanilines*, is derived from this hydrocarbon. Triphenylmethane itself is not employed as a basis for their preparation, simpler substances convertible into its derivatives being employed. The formation of the dyestuff involves three stages, *malachite-green* furnishing an example.

Heating benzaldehyde and dimethylaniline with zinc chloride forms *tetramethyldiaminotriphenylmethane*:



The carbon atom of the aldehyde group becomes the "methane carbon atom" of triphenylmethane.

The product also is termed *leucomalachite-green*. In hydrochloric-acid solution it is converted by oxidation with lead peroxide into the corresponding carbinol, $C_6H_5C[C_6H_4N(CH_3)_2]_2$ (OH), a colourless crystalline substance, like the parent leuco-compound. Being an amino-base, it is capable of dissolving in acids to form salts, these derivatives being colourless. Warming such a solution eliminates water, and produces the deep-green dyestuff, its double salt with zinc chloride, or the oxalate, being known as *malachite-green*. The elimination of water can be represented in several ways but usually is supposed to accord with the equation



Quinonoid form

This "quinonoid reaction" is analogous to the formation of the deep-yellow benzoquinone from the colourless quinol.

The three stages necessary to the formation of the dyestuff can be defined as follows:

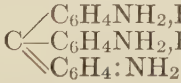
1. Formation of a *leuco-base* (colourless), a derivative of

$$HC(C_6H_4NH_2)_3.$$

2. Formation of a *colour-base* (colourless), a derivative of

$$HO\cdot C(C_6H_4NH_2)_3.$$

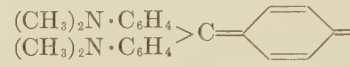
3. Formation of the *dyestuff*, a derivative of



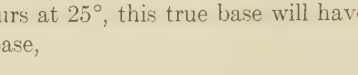
Reduction reconverts the dyestuffs into their leuco-bases, two hydrogen atoms being added during the reaction.

Crystal-violet or *hexamethyltriaminotriphenylmethane* furnishes an excellent example of a phenomenon also exhibited by other analogous basic substances. After the addition of an equivalent quantity of an alkali to a salt of crystal-violet, the liquid still remains coloured, has a strong alkaline reaction, and conducts an electric current. In course of time, the solution slowly becomes colourless, the change being attended by the disappearance of the alkalinity, and by a fall in the electric conductivity to that of the alkali-metal salt present. The liquid now contains a colour-base. These

phenomena are analogous to the conversion of acids into *pseudo*-acids (**322**), and for this reason the colour-base can be regarded as a pseudo-*base*. The initial product of the addition of the equivalent quantity of sodium hydroxide to crystal-violet is a solution of the true base,

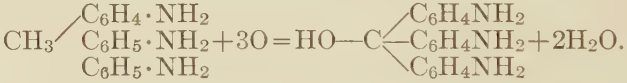


After several hours at 25°, this true base will have changed to the colour-base or *pseudo*-base,

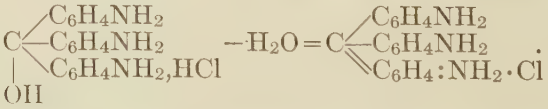


Hantzsch identified as *pseudo*-bases many substances other than that mentioned here.

Pararosaniline is obtained by the oxidation of a mixture of *p*-toluidine (one gramme-molecule) and aniline (two gramme-molecules) by arsenic acid or nitrobenzene, the methyl-group of toluidine furnishing the " methane carbon atom " of the triphenylmethane:



This colour-base dissolves in acids to form a red dyestuff, and can be reprecipitated by alkalis. Reduction with zinc-dust and hydrochloric acid transforms it into *paraleucaniline*, $HC(C_6H_4NH_2)_3$, a colourless crystalline substance melting at 148°, and reconverted into the colour-base by oxidation. The constitution of paraleucaniline is indicated by the formation of triphenylmethane through elimination of its amino-groups by diazotization. Inversely, paraleucaniline can be obtained by the nitration of triphenylmethane, and subsequent reduction of the trinitro-derivative. Paraleucaniline is converted by oxidation into triaminotriphenylcarbinol, and like malachite-green, that substance forms the dyestuff by elimination of water under the influence of acids:



Another important dyestuff related to triphenylmethane is *rosaniline*. Its preparation is effected similarly by oxidizing a mixture in equi-molecular proportions of aniline, *o*-toluidine, and *p*-toluidine with

arsenic acid, mercuric nitrate, or nitrobenzene. In this reaction the methane carbon atom is obtained from *p*-toluidine in accordance with the equation

$$\underset{p\text{-Toluidine}}{NH_2\cdot C_6H_4\cdot CH_3}+\underset{o\text{-Toluidine}}{C_6H_4(CH_3)NH_2}+C_6H_5\cdot NH_2+$$

$$+3O=2H_2O+HO\cdot C\begin{cases}C_6H_3<\begin{matrix}CH_3\\NH_2\end{matrix}\\C_6H_4NH\\C_6H_4NH_2\end{cases}\rightarrow C\begin{cases}C_6H_3<\begin{matrix}CH_3\\NH_2\end{matrix}\\C_6H_4NH_2\\C_6H_4{:}NH_2\cdot Cl\end{cases}\cdot$$

Colour-base Magenta

The chloride formed from the rosaniline colour-base by combination with one equivalent of hydrogen chloride and elimination of one molecule of water is termed *magenta*. This substance forms beautiful green crystals of metallic lustre, yielding with water a solution of an intense deep-red colour.

The colour of the magenta solution is due to the univalent cation, $(C_{20}H_{20}N_3)^{\cdot}$, such solutions being ionized almost completely, as is indicated by the slight increase in their molecular conductivity caused by further dilution. In addition, the solutions of all the magenta salts, such as the chloride, the bromide, and the sulphate, exhibit the same absorption-spectrum for solutions of equimolecular concentration, a token of the presence of a constituent common to all of them, the cation.

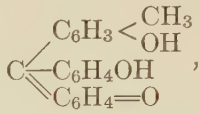
The salts with three equivalents of acid are yellow, the red univalent cation having been converted into the yellow tervalent cation, for solution of magenta in excess of hydrochloric acid yields a nearly colourless solution. These salts are hydrolyzed very readily, the red colour reappearing as the acid solution is poured into a great excess of water.

Many derivatives of pararosaniline and rosaniline with the hydrogen atoms of the amino-group replaced by alkyl-radicals are known, and each of them is a dyestuff. The violet colour becomes deeper with increase in the number of methyl-groups (341). *Pentamethylpararosaniline* has the trade-name "methyl-violet." Replacement by phenyl of one hydrogen atom in each of the amino-groups of rosaniline forms a blue dyestuff termed "aniline-blue."

Methyl-violet is obtained by the oxidation of dimethylaniline with potassium chlorate and cupric chloride, the methane carbon atom being derived from one of the methyl-groups.

Aniline-blue or *triphenylrosaniline hydrochloride* is formed by heating rosaniline with aniline and a weak acid such as benzoic acid, the amino-groups in the rosaniline being replaced by anilino-groups, and the liberated ammonia combining with the acid. This process is analogous to the formation of diphenylamine from aniline hydrochloride and aniline (298).

Dyestuffs formed from hydroxyl-derivatives of triphenylmethane are known also, but the difficulty of fixing them renders them much less valuable than those described. *Rosolic acid,*



obtained from rosaniline by diazotization, is an example of such dyestuffs.

Malachite-green and the pararosaniline and rosaniline dyestuffs colour wool and silk directly, and calico after mordanting (374).

The phthaleins (348) also are dyestuffs related to triphenylmethane.

Relation of Colour to Constitution.

374. The colour exhibited by a great variety of compounds is conditioned first of all by the atoms constituting the molecule. The alkali-metal salts of colourless acids are colourless also, copper salts are blue or green, and ferric salts are yellowish-red. Chloroform is colourless, iodoform is yellow, and so on.

Colour also is associated closely with the structure of the molecules, one isomeride often being colourless, and another intensely coloured. Owing to the great technical importance of dyestuffs, numerous researches on the relation between colour and constitution have been undertaken with the object of ascertaining the directions most likely to lead to success in the search for new dyestuffs. The goal of being able to predict from its structure whether an unsynthesized compound would be coloured, and what the colour would be, is still far from attainment. Although many rules have been established for specific classes of related compounds, only that of Witt, discussed later, possesses the character of a general law.

Substitution of the hydrogen atoms of a coloured substance by other atoms or groups may be attended by a deepening of the colour; that is by a displacement towards the violet region of the spectrum or *bathochromic* effect. In the reverse transformation the colour becomes lighter, the effect being termed *hypsochromic*. This phenomenon is quite distinct from the *intensity* of a colour; the preparation of a solution of given intensity from each of two substances of similar colour may require a much greater proportion of one than of the other.

Colour change is associated with displacement of the absorption-bands in the spectrum, deepening of the colour being due to displacement

towards the red end. When the transposition is so great as to bring the absorption-bands into the infra-red region, the absorption-bands originally located in the ultraviolet portion may be transposed to the visible part of the spectrum, a hypsochromic effect being induced with the development of what is termed a "Colour of the second order." This phenomenon furnishes an explanation of the apparently abnormal lightening of the colour through the introduction of new chromophores into a compound.

As long ago as the year 1868 GRAEBE and LIEBERMANN noted the invariable unsaturation of coloured compounds, and the disappearance of the colour as the result of saturation. In contrast to this observation is the existence of many colourless unsaturated compounds. The theory promulgated by WITT in 1876 affords a better insight into the problem. Hydrocarbons normally colourless become coloured on the introduction into them of certain groups such as the azo-group —N=N—, although sometimes the colour is only faint. He named such groups *chromophores*. When a second group of acidic or basic character is introduced into the molecule, the colour is developed, such groups being termed *auxochromes*. Nitrobenzene contains the chromophoric nitro-group, but has only a pale-yellow colour. Introduction of the auxochromic amino-group yields one of the deep-yellow nitroanilines.

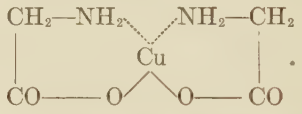
An auxochrome can exert a bathochromic effect or a hypsochromic effect; but in addition this type of group often exhibits another influence of great importance in technical practice, the conversion of a *coloured substance* into a *dyestuff*. Compounds of this class have the property of dyeing animal fibres such as wool and silk, or vegetable fibres such as cotton and linen, so that the colour is too fast to admit of removal by washing either with water alone or in conjunction with soap. Auxochromes are therefore also *tinctophores*.

It is desirable to draw attention to certain points respecting the process of dyeing. It is often sufficient to immerse the silk, wool, or cotton in a solution of the dyestuff. Although initially dissolved in water, the dye cannot be removed after dyeing by washing the fabric. Various theories in explanation of this phenomenon have been suggested. In some instances the dyestuff forms a solid solution with the fabric ("Inorganic Chemistry," 262), becoming distributed between the water and the material as between two immiscible substances, and an equilibrium being attained. With other types of dyeing adsorption comes into play.

When immersed in a solution of a dyestuff, a fabric does not necessarily become coloured. It is then imperative for the material to undergo a process termed "Mordanting," a substance being deposited in it to "Fix" the dyestuff, since it is incapable of uniting with the fibres directly. These

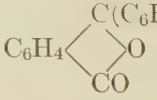
compounds are termed "Mordants," and normally are salts of weak bases or of acids. Examples are aluminium acetate, ferric salts, and tin compounds such as "Pink salt," $SnCl_4,2NH_4Cl$. The woven material is soaked thoroughly in a solution of one of these salts, and after complete penetration is exposed to the action of steam at a high temperature. The salt undergoes hydrolytic dissociation, and the base or acid, such as aluminium hydroxide or stannic acid, is deposited in a fine state of division on the fabric. The dyestuff unites with this base or acid, forming an insoluble, coloured compound not removable by washing. *Direct* dyestuffs are those capable of dyeing the fabric without preliminary mordanting.

Werner demonstrated the constitution of a great number of mordant dyestuffs to be characterized by the possession of a salt-forming group, and also by the presence of a second group capable of uniting with the secondary valencies ("Inorganic Chemistry," 330) of the metallic atom of the mordant. These secondary valencies are so situated as to facilitate the formation of an inner metallic complex salt with a structure similar to that assumed for the copper salt of glycine, and are denoted in the formula by dotted lines:

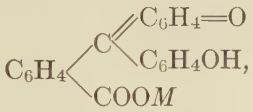


The formation of a ring denotes the secondary valencies to be subject to the operation of the same laws as the primary valencies, and indicates dyestuffs requiring a mordant for fixation normally to have such a constitution as will enable the metallic atom to take its place in a ring of five or six members.

The auxochromes include the hydroxyl-group, OH; the amino-group, NH_2; the carboxyl-group, COOH; the sulpho-group, SO_3H; and other groups. Among the chromophores are the nitro-group NO_2; the azo-group, —N=N—; the nitroso-group, NO; and the quinonoid-group, . So many coloured substances contain the quinonoid-group as to have engendered a belief in its presence in all such compounds. Numerous examples of the formation of coloured bodies through the transformation of benzene derivatives into quinonoid forms actually have been observed. One already cited (337) is the formation of salts by nitrophenol. Another is the conversion of colourless phenophthalein into its red metallic derivatives (348). In its colourless condition this indicator is a lactone of the formula



but its red salts contain a carboxyl-group and a quinonoid-group, and correspond with the formula



M representing a univalent metallic atom. On liberation by acids, phenolphthalein instantly assumes the colourless lactone form. The *pseudo*acids behave similarly, but the transformation is much less rapid.

The remarkably intense colour of the rosanilines cannot be ascribed merely to the presence of a quinonoid-group, but depends on the co-existence in a single molecule of both a quinonoid-group and unchanged benzene-nuclei. Quinhydrone (338) furnishes an analogous example. Quinol is colourless, and quinone is yellow; but quinhydrone, composed from a molecule of each, has a very intense dark colour.

The formation of colour is not caused always by the development of a quinonoid-form, as was noted by VON BAEYER. The deeply coloured salts of trianisylcarbinol, $(CH_3O \cdot C_6H_4)_3C \cdot OH$, and of similar compounds, certainly lack the quinonoid character. The explanation of this type of colour formation is probably to be sought in still obscure alterations in the positions of the atoms in the molecules. The phenomenon is termed *halochromy*.

Triphenylmethyl and Other Compounds with Free Linkings.

375. GOMBERG investigated the action of zinc on a benzene solution of *triphenylchloromethane*. He noted the separation of zinc chloride, and the presence in the solution of a compound precipitated by the addition of acetone or of ethyl formate. He regarded this compound as *triphenylmethyl*, $(C_6H_5)_3C—$, with one free valency. Its power of forming addition-products is remarkable. It is oxidized instantaneously by atmospheric oxygen to a *peroxide*,

$$(C_6H_5)_3C—O—O—C(C_6H_5)_3.$$

It decolorizes iodine solution immediately, forming *triphenylmethyl iodide*. With ether and many other compounds it yields addition-products.

A close investigation of triphenylmethyl revealed the existence of two forms, one being colourless and the other yellow. The solid colourless hydrocarbon is converted by solution into the yellow isom-

eride, the only highly reactive form. In solution the two modifications attain an equilibrium dependent on the temperature and on the nature of the solvent. As the molecular weight indicated by the cryoscopic method corresponds with nearly twice the empirical formula, the equilibrium

$$\underset{\text{Triphenylmethyl}}{2(C_6H_5)_3C} \rightleftarrows \underset{\text{Hexaphenylethane}}{(C_6H_5)_3C\cdot C(C_6H_5)_3}$$

requires the presence of a small percentage only of the yellow modification.

The colourless form consists of *hexaphenylethane*, and the yellow isomeride of triphenylmethyl. In *tridiphenylmethyl*, $(C_6H_5\cdot C_6H_4)_3C$, the unimolecular form predominates strongly, the solution having an intense violet colour. These compounds recall the parallel instance of nitrogen peroxide, known in a colourless form, N_2O_4, and in a yellowish-brown modification, NO_2. Like triphenylmethyl, the simpler form of nitrogen peroxide is characterized by its abnormal condition of unsaturation.

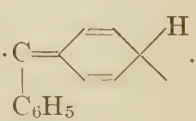
Some examples of hexaphenylethane derivatives lacking any direct relationship between the concentration of the unimolecular form in solution and the colour are known. For solutions of *bis*-2:5-*dimethoxyhexaphenylethane*,

$$(CH_3O)_2C_6H_3\cdot (C_6H_5)_2C\cdot C(C_6H_5)_2\cdot C_6H_3(OCH_3)_2,$$

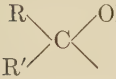
cryoscopic measurements have indicated the concentration of the unimolecular form at 53°, the freezing-point of *p*-dichlorobenzene, to be only a few units per cent. more than at 5·8°, the freezing-point of nitrobenzene; although the colour-intensity of the solutions at 53° is several times as strong as at 5·8°. When a solution of such a hexaphenylethane derivative is diluted at constant temperature, the colour-intensity similarly increases much more rapidly than the dissociation.

In such instances Gomberg has assumed the colour to be due to the presence of a quinonoid form, there being in solution an equilibrium between two isomerides:

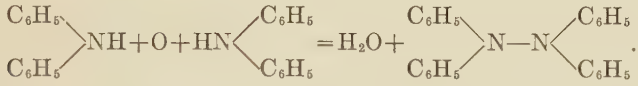
$$(C_6H_5)_2(CH_3O)_2C_6H_3\cdot C \rightleftarrows (CH_3O)_2C_6H_3\cdot \underset{\displaystyle C_6H_5}{\underset{|}{C}}=$$

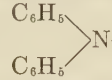


Besides this equilibrium, the unimolecular form is also in equilibrium with the bimolecular form.

The discovery of a compound with a free carbon valency by this research was followed by that of a number of other compounds of similar character. Contact with potassium develops a very intense colour in an ethereal solution of an aromatic ketone such as benzophenone, the change probably being occasioned by the formation of a compound of the formula  . The unchanged boiling-point of the liquid after complete solution of the potassium indicates the presence of the same number of molecules, and is an argument against the double formula. Such compounds also are oxidized instantly by contact with air.

Compounds containing a bivalent nitrogen atom with a free valency have been prepared also. Oxidation of diphenylamine yields *tetraphenylhydrazine:*



At 90° the solution of this compound in toluene dissociates, although only to a slight extent. The free *diphenylnitrogen*,  , is much less stable than triphenylmethyl. Its hot solution combines quantitatively with nitric oxide to form *diphenylnitrosoamine*, and with triphenylmethyl it yields a compound of the formula $(C_6H_5)_3C—N(C_6H_5)_2$.

Like triphenylmethyl, the free compounds $R_2N—$ are intensely coloured. The solution of *tetra-anisylhydrazine*,

$$(CH_3O\cdot C_6H_4)_2N—N(C_6H_4\cdot OCH_3)_2,$$

illustrates this characteristic. At the ordinary temperature it is almost colourless; on warming, it becomes deep green; on cooling, the colour vanishes.

According to the law of Beer, solutions containing the same quantity of colouring matter in different amounts of the solvent exhibit the same light absorption when the thickness of the liquid layer is inversely proportional to the concentration, for under these conditions the light in transit encounters the same number of molecules of colouring matter. For dissociated substances the law does not hold, as the degree of dissociation varies with the dilution. On this fact is based a method of measuring the extent of dissociation. Its application to tetra-anisylhydrazine proved a 0·05 per cent. solution in benzene to be 3·2 times as much dissociated as a 0·3 per cent. solution in the same solvent.

as-*Diphenylhydrazine* reacts with picryl chloride to form 1:1-*diphenyl-2-trinitrophenylhydrazine* (I):

$$\begin{matrix}C_6H_5\\C_6H_5\end{matrix}\!\!>N\cdot NH_2+Cl\cdot C_6H_2(NO_2)_3 \rightarrow \underset{\text{I.}}{\begin{matrix}C_6H_5\\C_6H_5\end{matrix}\!\!>N\cdot NH\cdot C_6H_2(NO_2)_3}+HCl \rightarrow$$

$$\rightarrow \underset{\text{II.}}{\begin{matrix}C_6H_5\\C_6H_5\end{matrix}\!\!>N\cdot N\cdot C_6H_2(NO_2)_3}.$$

When 1:1-diphenyl-2-trinitrophenylhydrazine is oxidized with lead peroxide, the hydrogen of the NH-group is abstracted, with formation of 1:1-*diphenyl-2-trinitrophenylhydrazyl* (II), a substance not exhibiting any tendency to unite with itself. It consists of dark-violet crystals like those of potassium permanganate; and whilst tetraphenylhydrazine undergoes but slight dissociation, this substance furnishes an example of a compound only obtained in its unimolecular form.

Dibenzyl and its Derivatives.

376. *Dibenzyl*, $C_6H_5\cdot CH_2\cdot CH_2\cdot C_6H_5$, can be obtained by the action of sodium on benzyl chloride:

$$C_6H_5\cdot CH_2\boxed{Cl+Na_2+Cl}CH_2\cdot C_6H_5=C_6H_5\cdot CH_2\cdot CH_2\cdot C_6H_5+2NaCl.$$

This method of formation indicates it to be *symmetrical diphenylethane*. It melts at 52°.

Symmetrical diphenylethylene, $C_6H_5\cdot CH{:}CH\cdot C_6H_5$, melts at 125°, and is termed *stilbene*. It can be obtained by various methods, one being the decomposition by heat of an aqueous solution of phenylsodionitromethane into stilbene and sodium nitrite:

$$2C_6H_5\cdot CH{:}NO\cdot ONa=C_6H_5\cdot CH{:}CH\cdot C_6H_5+2NaNO_2.$$

With bromine stilbene forms an addition-product convertible into *tolan*, $C_6H_5\cdot C{\equiv}C\cdot C_6H_5$, by elimination from each molecule of two molecules of hydrogen bromide. Tolan can be reconverted into stilbene by gentle reduction.

p-*Diaminostilbene*, $NH_2\cdot C_6H_4\cdot CH{:}CH\cdot C_6H_4\cdot NH_2$, can be obtained by the interaction of *p*-nitrobenzyl chloride, $ClH_2C\cdot C_6H_4\cdot NO_2$, and alcoholic potassium hydroxide, with subsequent reduction of the p-*dinitrostilbene*, It is employed as a basis for the preparation of certain dyestuffs.

Derivatives of dibenzyl are produced by the condensation of benzaldehyde in presence of potassium cyanide, *benzoin* being formed in accordance with the equation

$$C_6H_5\cdot C\begin{matrix}H\rightarrow O\\O+H\end{matrix}C\cdot C_6H_5=C_6H_5\cdot CO\cdot \underset{\text{Benzoin}}{CHOH}\cdot C_6H_5.$$

It has the character of a keto-alcohol, adding two hydrogen atoms to form the dihydric alcohol *hydrobenzoin*, $C_6H_5 \cdot CHOH \cdot CHOH \cdot C_6H_5$. Its oxidation gives the diketone *benzil*, $C_6H_5 \cdot CO \cdot CO \cdot C_6H_5$. Benzoin contains the group —CHOH·CO— present in the carbohydrates (**203**). It possesses also characteristic carbohydrate properties, reducing an alkaline copper solution, and yielding an osazone.

Benzil is a yellow crystalline substance. As a diketone it unites with two molecules of hydroxylamine to form a dioxime.

Heating with alcoholic potassium hydroxide causes benzil to combine with one molecule of water, and to undergo an intramolecular transformation to *benzilic acid*, a reaction analogous to the formation of pinacolin from pinacol (**150**):

$$C_6H_5 \cdot CO \cdot CO \cdot C_6H_5 + H_2O = \underset{\text{Benzilic acid}}{\overset{C_6H_5}{C_6H_5} > C < \overset{OH}{COOH}}.$$

CONDENSED BENZENE-NUCLEI.

377. *Condensed-ring compounds* contain two or more closed chains, with carbon atoms common to each. Such substances are present in the higher-boiling fractions of coal-tar (283). Next to the phenols, *naphthalene* is the principal constituent of the second fraction or carbolic oil, and of the third fraction or creosote-oil. The anthracene-oil contains *anthracene, phenanthrene,* and other hydrocarbons. These three compounds and some of their derivatives will be described.

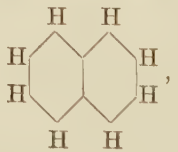
I. NAPHTHALENE, $C_{10}H_8$.

Naphthalene is present in considerable proportion in coal-tar, and is obtained from it readily in the pure state. Cooling precipitates crude crystals of naphthalene from the fraction distilling between 170° and 230°. Part of the liquid impurities are expressed, the remainder being eliminated by conversion into non-volatile sulphonic acids through warming the crude product with small proportions of concentrated sulphuric acid, and distilling with steam or subliming. The product is pure naphthalene.

Naphthalene crystallizes in shining plates, melting at 80°, and boiling at 218°. It is insoluble in water, but soluble readily in hot alcohol and ether, and to a very small extent in cold alcohol. It has a characteristic odour, and is very volatile. It is present always in coal-gas, the illuminating power of the fish-tail burner being dependent mainly on its presence. It is employed extensively in the manufacture of dyestuffs.

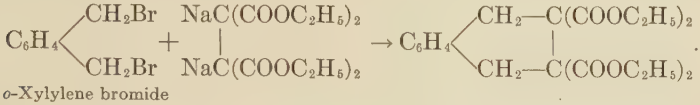
The formation of naphthalene by the passage of the vapours of many compounds through a red-hot tube is a process somewhat similar to that in the retorts of the gas-works (283), and explains its occurrence in coal-tar.

The constitution of naphthalene is indicated in 355 to be



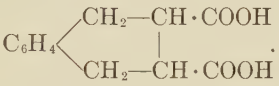
a view confirmed by two syntheses.

1. *o*-Xylylene bromide is converted by tetraethyl disodioethanetetracarboxylate into *tetraethyl hydronaphthalenetetracarboxylate*:



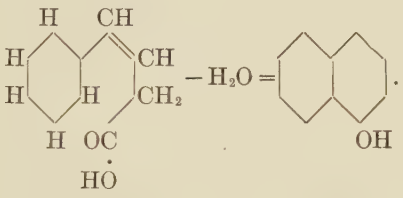
o-Xylylene bromide

Saponification of this compound expels from each molecule two molecules of carbon dioxide, forming *hydronaphthalenedicarboxylic acid*:

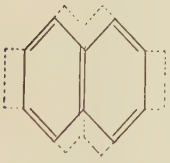


The silver salt of this acid gives up two molecules of carbon dioxide and two atoms of hydrogen readily, yielding naphthalene.

2. Heating phenylvinylacetic acid converts it into *α-naphthol*, a hydroxy-derivative of naphthalene:

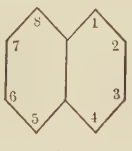


Phenylvinylacetic acid α-Naphthol



I.

Fig. 76.—Thiele's Naphthalene-formula.



II.

Fig. 77.—Simple Naphthalene-formula.

Naphthalene has all the characteristics of an aromatic hydrocarbon. With nitric acid it yields a nitro-derivative; with sulphuric acid a sulphonic acid; its hydroxyl-derivatives have the phenolic character; the amino-compounds undergo the diazo-reaction; and so on.

For naphthalene, as for benzene (287), no formula indicating its internal structure and satisfactorily accounting for its properties has been proposed.

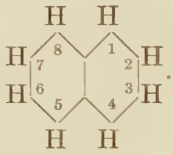
Thiele suggested formula I (Fig. 76), with inactive double bonds

(287), and of those proposed it seems to give the best expression to the properties of naphthalene. The identity of the formula representing most accurately the internal structure of the naphthalene molecule is of no practical importance, for although the simple scheme II (Fig. 77) leaves the problem unsolved, it accounts fully for the isomerism of the derivatives of naphthalene.

As with benzene, partial hydrogenation of naphthalene changes its characteristic aromatic character, *naphthalene dihydride*, $C_{10}H_{10}$, adding bromine as readily as compounds with double bonds.

378. Naphthalene yields many more substitution-products than benzene, the number obtained corresponding with those theoretically possible for a compound with the formula in **377**. This fact supports the adoption of the constitution indicated.

A compound of the formula



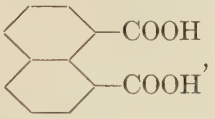
must yield two isomeric monosubstitution-products. Substitution can be at a carbon atom in direct union with one of the two carbon atoms common to both rings (1, 4, 5, or 8), or at one of the other similar carbon atoms (2, 3, 6, or 7). Two series of monosubstitution-products are known, those with the hydrogen at 1, 4, 5, or 8 replaced being denoted as α-derivatives, and those with hydrogen substituted at 2, 3, 6, or 7 being termed β-derivatives.

A great number of disubstitution-products is possible. For two similar substituents it is ten, and for two dissimilar substituents fourteen. Many of them have been prepared. The ten isomerides are distinguished by the numbers

1:2, 1:3, 1:4, 1:5, 1:6, 1:7, 1:8, 2:3, 2:6, 2:7.

In any other arrangement the grouping is identical with one of these pairs of positions, exemplified by the equivalence of 2:5 and 1:6, and of 3:6 and 2:7. For three similar substituents the number of possible isomerides is much greater, and still greater for three dissimilar substituents. The disubstitution-products with the substituents in the same ring are termed *ortho*, *meta*, and *para*. When they are in different rings, the derivatives usually are distinguished by numbers, or sometimes by letters, a compound 4:5 also being denoted as $\alpha\alpha'$, and one 3:6 as $\beta\beta'$. The positions 1:8 and 4:5 are named also the *peri*-posi-

tions, and in certain respects resemble the *ortho*-positions, peri-*naphthalenedicarboxylic acid,*



recalling *o*-phthalic acid in its ability to form an anhydride.

The great number of isomerides sometimes renders the orientation of naphthalene derivatives difficult, and the positions of the substituents in many compounds are still uncertain. The method of orientation employed is similar to that for the benzene derivatives, involving the conversion of compounds with side-chains in unknown positions into others with substituents in ascertained positions.

Oxidation is another important aid in their orientation, being employed to determine whether the substituents are attached to the same ring, or to different rings, and to identify their relative positions. The procedure is exemplified by the determination of the positions of the nitro-groups in a dinitronaphthalene. If it yield phthalic acid by oxidation, the two nitro-groups must be in union with the same ring, that removed by the oxidation. The formation of a dinitrophthalic acid indicates the two nitro-groups to be united with the same ring, and the orientation of these groups in this acid should indicate their relative positions in the naphthalene derivative. Oxidation to mononitrophthalic acids demonstrates the presence of one nitro-group in each ring, and orientation of the mononitrophthalic acids will determine the position of either of the nitro-groups.

Substitution-products.

379. The homologues of naphthalene, such as the methyl-derivatives and ethyl-derivatives are unimportant. They can be prepared by the WURTZ-FITTIG method, or by that of FRIEDEL and CRAFTS (284, 1 and 2).

α-Methylnaphthalene is a liquid boiling at 240°–242°; *β-methylnaphthalene* is a solid melting at 32°. Both are present in coal-tar. Their oxidation yields *α-naphthoic acid* and *β-naphthoic acid*, derivatives resembling benzoic acid in their properties. The naphthoic acids are converted into naphthalene by distillation with lime.

α-Chloronaphthalene is formed by the action of chlorine on boiling naphthalene, and α-bromonaphthalene by employing bromine similarly. Although their halogen atom is not attached so firmly as that in monochlorobenzene or in monobromobenzene (289), they are not decomposed

by boiling with alkalis. A similar stability characterizes the corresponding β-compounds. They are not obtained by the direct action of halogens on naphthalene, but can be prepared from other β-compounds, such as amino-derivatives and sulpho-derivatives, by the methods described for benzene (**292** and **307**, 4).

The product obtained by the action of concentrated nitric acid on naphthalene is very important for the orientation of the naphthalene derivatives. It is *α-nitronaphthalene*, melting at 61°, and is proved to belong to the α-series by its conversion into a naphthol identical with that obtained from phenylvinylacetic acid (**377**).

The position of the substituents in a great number of monosubstitution-products can be determined from a knowledge of that of the nitro-group in this nitronaphthalene, for the nitro-group can be reduced to an amino-group replaceable by numerous atoms or groups through the diazo-reaction. A monosubstituted naphthalene being known to be an α-compound, its isomeride must belong to the β-series.

α-Nitronaphthalene is a yellow, crystalline compound, and melts at 61°. The corresponding β-compound is similar, and melts at 79°. It is obtained by diazotizing 2-*nitro-α-naphthylamine*.

Heating naphthalene with concentrated sulphuric acid at a temperature not exceeding 80° forms mainly *α-naphthalenemonosulphonic acid*. At 160° the β-acid is the principal product, owing to the conversion of the α-compound into its β-isomeride. Each is crystalline and very hygroscopic.

Fusion with sodium hydroxide or potassium hydroxide converts the naphthalenesulphonic acids into *naphthols*, $C_{10}H_7 \cdot OH$, with properties very similar to those of phenol. They are present in coal-tar. *α-Naphthol* melts at 95°, and boils at 282°; *β-naphthol* melts at 122° and boils at 288°. The hydroxyl-group in these compounds can be replaced much more readily than that in phenol. They dissolve in alkalis. With ferric chloride α-naphthol yields a flocculent violet precipitate; β-naphthol gives a green coloration, and a precipitate of *β-dinaphthol*, $HO \cdot C_{10}H_6 \cdot C_{10}H_6 \cdot OH$. The violet precipitate obtained with α-naphthol is possibly an iron derivative of α-dinaphthol. Its formation furnishes a test for contamination of the β-compound by its α-isomeride.

α-Naphthylamine and *β-naphthylamine*, $C_{10}H_7 \cdot NH_2$, can be obtained by the reduction of the corresponding nitro-derivatives, but usually are prepared by heating the corresponding naphthol with the ammonia compound of zinc chloride or of calcium chloride. α-Naphthylamine is a solid and is formed also by heating naphthalene with sodamide, NH_2Na, above 200°, hydrogen being evolved. It melts at 50°, and

has a fæcal-like odour; β-naphthylamine melts at 112°, and is nearly odourless. A mode of distinguishing between the isomerides is afforded by the blue precipitate with ferric chloride and other oxidizers given by the salts of the α-compound, but not by those of the β-compound.

These bases are of technical importance, the dyestuffs of the *congo-group* and the *benzopurpurins* being derived from them, and possessing the important property of dyeing unmordanted cotton.

Congo-red is formed by diazotizing benzidine, and bringing the product into contact with a sulphonic acid of naphthylamine. The dyestuff is the sodium salt of the acid formed:

$$H_2N\cdot C_6H_4{-}C_6H_4\cdot NH_2 \rightarrow Cl\cdot N_2\cdot C_6H_4{-}C_6H_4\cdot N_2\cdot Cl + 2C_{10}H_6{<}\begin{matrix}SO_3H\\NH_2\end{matrix} \rightarrow$$

Benzidine — Benzidinediazonium chloride — 1:4-Naphthylaminesulphonic acid

$$\rightarrow \begin{matrix}NaO_3S\\H_2N\end{matrix}{>}C_{10}H_5\cdot N{:}N\cdot C_6H_4\cdot C_6H_4\cdot N{:}N\cdot C_{10}H_5{<}\begin{matrix}SO_3Na.\\NH_2\end{matrix}$$

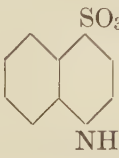
Congo-red

The acid itself is blue.

The benzopurpurins differ from congo-red only in having a methyl-group attached to each benzene-nucleus of the benzidine-group.

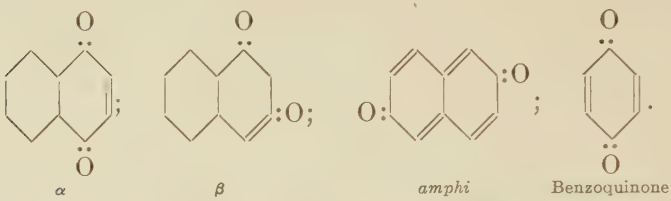
380. Among the polysubstituted naphthalene derivatives is 2:4-*dinitro-α-naphthol*, obtained by the action of nitric acid on the monosulphonic acid or disulphonic acid of α-naphthol. Its sodium salt is Martius's *yellow*, and dyes wool and silk directly a golden yellow. Nitration of α-naphtholtrisulphonic acid yields dinitronaphtholsulphonic acid, its potassium salt being *naphthol-yellow*. It resists the action of light better than Martius's yellow.

Naphthionic acid is one of the longest-known naphthalene derivatives. It is 1:4-*naphthylaminesulphonic acid*,



and is produced by the interaction of α-naphthylamine and sulphuric acid. It is crystalline, and is only slightly soluble in water. It is manufactured for the preparation of congo-red and other dyestuffs. Solutions of its salts display an intense reddish-blue fluorescence.

Three quinones of naphthalene are known:



α-Naphthaquinone, $C_{10}H_6O_2$, is formed by the oxidation of many α-derivatives, and of some di-derivatives, of naphthalene. Usually it is prepared from naphthalene by oxidation with a boiling solution of chromic acid in glacial acetic acid, a method of formation without parallel among those for the preparation of the corresponding benzene derivatives. It crystallizes from alcohol in deep-yellow needles melting at 125°. Oxidation converts it into phthalic acid, indicating both oxygen atoms to be attached to the same ring. With hydroxylamine it yields an oxime. A knowledge of the structure of α-naphthaquinone facilitates the determination of that of other di-derivatives. If oxidation yield this quinone by elimination of the substituents, they must be 1:4-derivatives.

β-Naphthaquinone, $C_{10}H_6O_2$, is formed by oxidation of 1:2-aminonaphthol.

amphi-*Naphthaquinone*, or 2:6-*naphthaquinone*, is obtained by oxidation of a benzene solution of the corresponding dihydroxynaphthalene with lead peroxide.

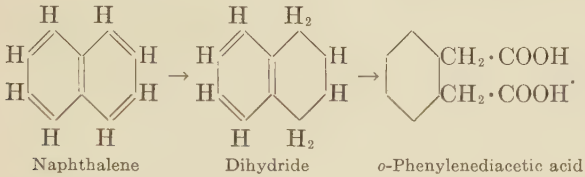
The structural formulæ indicate only the *amphi*-isomeride to have its carbonyl-groups placed relatively to the double bonds like those in benzoquinone, and these two quinones are very similar in chemical character. Each oxidizes instantly a cold dilute solution of hydrogen iodide, turns ferrous ferrocyanide blue, and oxidizes sulphurous acid. α-Naphthaquinone exhibits none of these characteristics, but resembles benzoquinone in odour and volatility. β-Naphthaquinone does not oxidize dilute hydrogen iodide, but turns ferrous ferrocyanide blue, and oxidizes sulphurous acid. Like the *amphi*-derivative, it is non-volatile, and therefore odourless. Each of the naphthaquinones has a red colour.

Addition-products.

381. Naphthalene and its derivatives yield addition-products somewhat more readily than the benzene derivatives.

All the intermediate hydrogenation-products of naphthalene from *dihydronaphthalene*, $C_{10}H_{10}$, to *decahydronaphthalene*, $C_{10}H_{18}$, are known,

each member having two hydrogen atoms more than its immediate predecessor. The first-named is obtained by the action of sodium and alcohol on naphthalene. Oxidation converts it into o-*phenylenediacetic acid*:

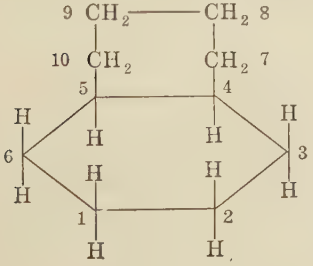


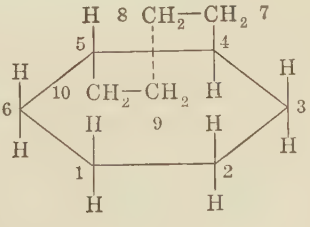
Assuming the formula given to represent naphthalene, the hydrogen is added to the conjugated double bond at the positions 1:4.

Tetrahydronaphthalene boils at 206°. It and decahydronaphthalene are manufactured by the hydrogenation of naphthalene with hydrogen at a pressure between ten and fifteen atmospheres in presence of finely-divided nickel as a catalyst. They have the trade-names "Tetralin" and "Dekalin," and are valuable solvents. They also find application as motor-fuels and as turpentine-substitutes.

Two isomeric modifications of decahydronaphthalene are present in the crude hydrogenation-product; they can be separated by fractional distillation. The *cis*-form boils at 193°, and its density is $D_4^{20}=0{\cdot}898$; the corresponding constants for the *trans*-form are 185° and 0·872. These two compounds are stereoisomerides. Adopting Mohr's method (**278**) for constructing models with strainless rings not having the carbon atoms of each *cyclo*hexane ring situated in the same plane, two spacial models are found to be possible. In the model of the *cis*-form the two hydrogen atoms attached to the common carbon atoms 4 and 5 lie in the same spacial segment; in that of the *trans*-form these hydrogen atoms are situated in different segments. The relative position of the two *cyclo*hexane rings formed by carbon atoms 1 to 6 and 5, 4, 7, 8, 9, and 10 is different in the two configurations.

Formulæ I and II give a graphical representation of these two forms. In Fig. 78 the two models are shown in perspective, the bond between the carbon atoms 4 and 5 common to both rings being denoted by a thick line:





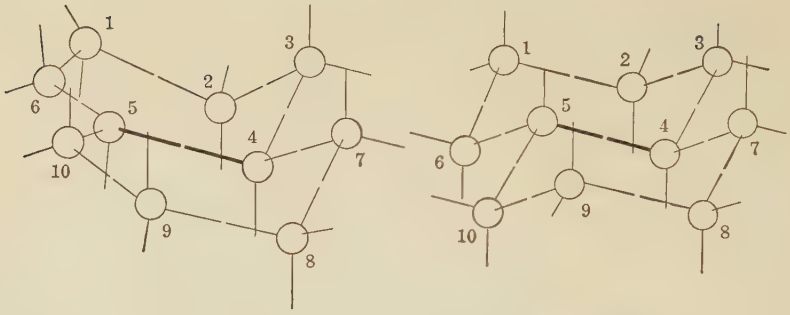
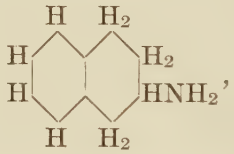


FIG. 78.—ISOMERISM OF DECAHYDRONAPHTHALENE.

Reduction with sodium and boiling amyl alcohol transforms β-naphthylamine into a *tetrahydride*, $C_{10}H_{11}\cdot NH_2$, a compound with most of the properties characteristic of the aliphatic amines. It is strongly alkaline, absorbs carbon dioxide from the air, has an ammoniacal odour, and cannot be diazotized. Each of the four hydrogen atoms is in union with the same ring as the amino-group,



for oxidation with potassium permanganate converts the compound into the *o*-carboxylic acid of dihydrocinnamic acid,

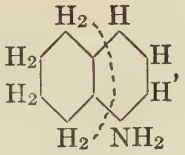
$$C_6H_4<\begin{matrix}CH_2\cdot CH_2\cdot COOH\\COOH\end{matrix},$$

a derivative necessarily formed by oxidation at the carbon atom in union with the amino-group from a tetrahydride with the structure indicated. Moreover, the hydrogen addition-product does not absorb bromine, additional evidence of the union of the four hydrogen atoms with the same benzene-nucleus. The entrance of two hydrogen atoms into each ring would produce a compound with double bonds, capable of yielding an addition-product with bromine.

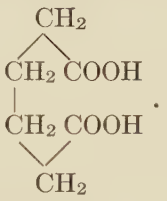
The reduction-product therefore may be regarded as benzene with a saturated side-chain, $—CH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_2—$, attached to two *ortho*-carbon atoms.

α-Naphthylamine can be reduced also by amyl alcohol and sodium, but the tetrahydride formed is different in character from that obtained

from β-naphthylamine, for it possesses all the properties characteristic of the aromatic amines, being diazotizable, and lacking the ammoniacal odour. As it resembles β-naphthylamine in its inability to form an addition-product with bromine, its constitution is



indicating the four hydrogen atoms in it also to be in union with the same nucleus, but not the one carrying the amino-group. In support of this view are its completely aromatic character, and the fact of the oxidation with potassium permanganate removing the ring with the amino-group to form adipic acid (**161**),



α-Naphthylamine tetrahydride therefore must be regarded as aniline with a saturated side-chain, $—CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2—$, in union with two *ortho*-carbon atoms.

The molecular refraction of benzylamine is 34·12, the calculated value being 34·30; the corresponding values for aniline are 30·27 and 29·72. These facts prove the refraction of benzylamine to be normal, but that of aniline to be abnormal, with an exaltation of 0·55. A similar discrepancy characterizes the reduction-products of α-naphthylamine and β-naphthylamine. The molecular refraction calculated for both is 45·80, the experimental value for the α-compound containing an aromatic amino-group being 46·66, and that for the β-compound, with an aliphatic amino-group, being 45·88. Only the amine of aromatic character exhibits an exalted molecular refraction. This example furnishes further evidence of the value of molecular refraction in deciding questions of structure.

II. ANTHRACENE, $C_{14}H_{10}$.

382. *Anthracene* is present only in small proportion in coal-tar, the amount varying between 0·25 and 0·45 per cent. Despite this fact, it is the basis of the manufacture of the important dyestuff alizarin (**385**).

The so-called " 50 per cent. anthracene," obtained from anthracene-oil (283), is distilled with one-third of its weight of potassium carbonate from an iron retort. Among the impurities thereby removed is *carbazole*, $\begin{matrix}C_6H_4\\ \\ C_6H_4\end{matrix}\!\!>\!NH$, a substance present in considerable proportion in the crude anthracene, it becoming converted into a non-volatile potassium derivative $(C_6H_4)_2N\cdot K$. The distillate consists almost entirely of anthracene and phenanthrene, the two substances being separated by dissolving the phenanthrene in carbon disulphide. Crystallization from benzene yields pure anthracene.

It crystallizes in colourless glistening leaflets with a fine blue fluorescence. It melts at 213°, and boils at 351°. It dissolves readily in boiling benzene, but with difficulty in alcohol and ether. With picric acid it gives a compound melting at 138°, of the formula

$$C_{14}H_{10}\cdot C_6H_2(NO_2)_3OH.$$

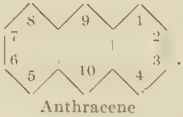
Exposure to light transforms anthracene into *dianthracene*, and in the dark this substance becomes depolymerized to anthracene. This change exemplifies the rare phenomenon of a reversible photochemical reaction:

$$2C_{14}H_{10} \underset{\text{Dark}}{\overset{\text{Light}}{\rightleftarrows}} C_{28}H_{20}.$$

Several modes of preparation affording an insight into the constitution of anthracene are known. One of them is its synthesis by Anschütz's method from benzene, aluminium chloride, and tetrabromoethane:

$$C_6H_6+\begin{matrix}BrCHBr\\ |\\ BrCHBr\end{matrix}+C_6H_6=C_6H_4\!\!<\!\!\begin{matrix}CH\\ |\\ CH\end{matrix}\!\!>\!C_6H_4+4HBr.$$

This synthesis indicates anthracene to contain two benzene-nuclei united by the group C_2H_2 through two *ortho*-carbon atoms of each nucleus, as is proved for anthraquinone in 383. Its constitutional formula is



Anthracene

Obviously, it must yield a very large number of isomeric substitution-products. Three monosubstitution-products are possible. Numbering the carbon atoms as in the formula, then 1 = 4 = 5 = 8, 2 = 3 = 6 = 7,

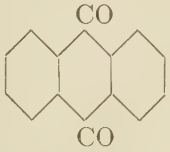
and 9 = 10. Fifteen disubstitution-products with similar groups are possible. A very considerable number of anthracene derivatives is known, although it is small in comparison with the enormous number theoretically possible.

The orientation of the anthracene derivatives is effected similarly to those of naphthalene (378), oxidation accompanied by a study of its products being an important aid.

Substitution-products.

383. *Anthraquinone*, $C_{14}H_8O_2$, is one of the most important derivatives of anthracene, and is obtained from it by oxidation with such agents as nitric acid and chromic acid. Anthracene is converted into anthraquinone by nitric acid so readily as to inhibit its nitration.

Anthraquinone is proved to have the structure



by its formation through the interaction of phthalic anhydride and benzene in presence of a dehydrator such as aluminium chloride:

$$C_6H_4<\begin{matrix}CO\\CO\end{matrix}>O + H_2 C_6H_4=C_6H_4<\begin{matrix}CO\\CO\end{matrix}>C_6H_4+H_2O.$$

Phthalic anhydride

The reaction takes place in two stages, *o*-benzoylbenzoic acid, $C_6H_4<\begin{matrix}CO\cdot C_6H_5\\COOH\end{matrix}$, being the initial product, and losing one molecule of water from each molecule to form anthraquinone:

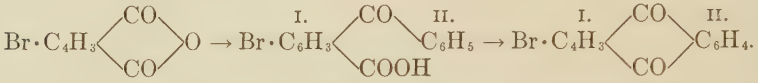
$$C_6H_4<\begin{matrix}CO\\ \diagup\diagdown C_6H_5\\COOH\end{matrix} - H_2O = C_6H_4<\begin{matrix}CO\\CO\end{matrix}>C_6H_4.$$

The constitutional formula of anthraquinone indicates only two isomeric monosubstitution-products to be possible, a conclusion verified by experiment. This fact furnishes additional evidence of the accuracy of the formula indicated.

The central groups in anthraquinone, and hence those in anthracene, can be demonstrated to be in union with two *ortho*-carbon atoms in each

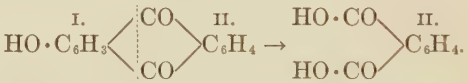
benzene-nucleus. The method is similar to that employed in proving the constitution of naphthalene (355), the marking of one of the nuclei by the introduction of a substituent affording a means of identifying the nucleus eliminated by oxidation.

Benzene and aluminium chloride react with *bromophthalic anhydride* as with phthalic anhydride, yielding *bromoanthraquinone* by elimination of water from the *bromobenzoylbenzoic acid* formed:



Bromophthalic anhydride — Bromobenzoylbenzoic acid — Bromoanthraquinone

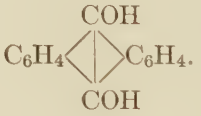
Bromoanthraquinone being a derivative of phthalic acid, its two carbonyl-groups must be united to two *ortho*-carbon atoms of nucleus I. Its bromine atom can be replaced by a hydroxyl-group by heating with potassium carbonate at 160°, and the *hydroxyanthraquinone* formed can be oxidized to phthalic acid by the action of nitric acid. These transformations prove nucleus II to be unattacked, and to have its two carbonyl-groups attached to *ortho*-carbon atoms:



Hydroxyanthraquinone — Phthalic acid

384. Anthraquinone crystallizes from glacial acetic acid in light-yellow needles melting at 277°. At higher temperatures it sublimes very readily, forming long sulphur-yellow prisms. It is very stable, and is not attacked easily by oxidizers, or by concentrated nitric acid or sulphuric acid.

In some measure the name anthra*quinone* is incorrect, for this substance lacks some of the properties characteristic of quinones, such as ready reducibility, great volatility, and pungent odour, being much more like a diketone. With fused potassium hydroxide it yields benzoic acid, and with hydroxylamine an oxime. Warming it with zinc-dust and sodium-hydroxide solution gives the disodium-derivative of *anthraquinol*,

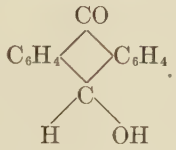


Anthraquinol forms brown crystals melting at 180°, its solutions exhibiting an intense green fluorescence. Its alkaline solution has a deep

blood-red colour, and in this condition it is converted into anthraquinone by atmospheric oxidation.

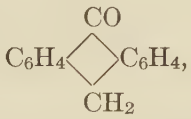
This property of anthraquinol makes its formation a delicate test for anthraquinone. The examination of the substance is effected by warming it with zinc-dust and sodium-hydroxide solution. In presence of anthraquinone, a blood-red coloration is developed, and is destroyed by agitating the mixture with air.

Isomeric with anthraquinol is the ketonic compound *oxanthrone*,

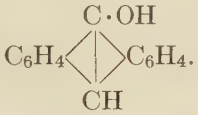


It is converted by a cold alcoholic solution of hydrogen chloride into anthraquinol to the extent of 97 per cent., the same reagent effecting the inverse transformation of anthraquinol into oxanthrone to the extent of 3 per cent. Oxanthrone melts at 167°, is colourless, and does not exhibit fluorescence in solution. Anthraquinol and oxanthrone exemplify a type of desmotropy characterized by the great stability of both forms.

Reduction of anthraquinone with tin and hydrochloric acid gives *anthrone*,



a substance transformed by boiling with alkalis into the tautomeric *anthranol*,



In solution, anthranol exhibits a bright-blue fluorescence. It is reconverted readily into anthrone, and anthranol also is produced to some extent by boiling anthrone with dilute acetic acid. Anthrone is to be regarded as a *pseudo*-acid, anthranol being its *aci*-form.

Stronger reduction of anthraquinone by heating with zinc-dust yields anthracene.

385. *Alizarin* or *dihydroxyanthraquinone*, $C_{14}H_6O_2(OH)_2$, is the most important derivative of anthraquinone, and is a dyestuff of a splendid red colour. Formerly it was manufactured from madder-

root, a substance containing the glucoside *ruberythric acid*, $C_{26}H_{28}O_{14}$. Boiling with dilute sulphuric acid or hydrochloric acid transforms this glucoside into dextrose and alizarin:

$$\underset{\text{Ruberythric acid}}{C_{26}H_{28}O_{14}} + 2H_2O = 2\underset{\text{Dextrose}}{C_6H_{12}O_6} + \underset{\text{Alizarin}}{C_{14}H_6O_2(OH)_2}.$$

The dyestuff is produced now almost wholly by a synthetic method. It is one of the organic dyestuffs known in antiquity.

The first step in preparing alizarin is to oxidize the anthracene to anthraquinone with sodium dichromate and sulphuric acid. Heating with concentrated sulphuric acid at 100° converts various impurities into sulphonic acids, the anthraquinone remaining unchanged; and dilution dissolves these sulphonic acids, pure anthraquinone being left after filtering. The quinone is heated at 160° with fuming sulphuric acid containing fifty per cent. of sulphur trioxide, the main product being the monosulphonic acid.

> The presence of a mercury salt induces the formation of the α-sulphonic acid, but in its absence between 98 and 100 per cent. of the β-sulphonic acid is formed at 156°. Addition of even so small a proportion as 0·035 per cent. of mercuric sulphate lowers this figure to 61 per cent.; whilst one per cent. of this salt reduces the yield of the β-acid to 16·3 per cent., and simultaneously gives 83·7 per cent. of the α-compound. Catalysts very rarely exert an influence of this remarkable type.

The sodium salt of the sulphonic acid is only slightly soluble in water, and separates after neutralization of the acid with sodium carbonate. Fusion with sodium hydroxide replaces the sulpho-group by hydroxyl. A second hydroxyl-group is formed simultaneously, its production being facilitated considerably by the addition to the reaction-mixture of potassium chlorate as an oxidizer:

$$C_6H_4\!<\!\begin{matrix}CO\\CO\end{matrix}\!>\underset{\substack{\text{Sodium anthraquinone-}\\\text{monosulphonate}}}{C_6H_3\cdot SO_3Na} + 3NaOH + O =$$

$$= C_6H_4\!<\!\begin{matrix}CO\\CO\end{matrix}\!>C_6H_2(ONa)_2 + 2H_2O + Na_2SO_3.$$

The dyestuff is liberated from the sodium salt by addition of an acid.

Anthraquinone can be oxidized to alizarin directly by heating it with very concentrated aqueous alkali in presence of oxidizers such as mercuric oxide and potassium chlorate.

Alizarin crystallizes in red prisms, and sublimes in orange needles, melting at 289°. It is almost insoluble in water, and slightly soluble in alcohol. On account of its phenolic character, it dissolves in alkalis. It yields a diacetate. Distillation with zinc-dust converts it into anthracene, and this reaction gave the first insight into the constitution of alizarin.

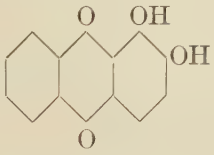
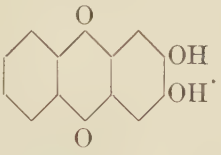
The value of alizarin as a dyestuff depends on its power of forming with metallic oxides fine-coloured insoluble compounds termed *lakes*. When a fabric is mordanted with one of these oxides, it can be dyed with alizarin, the colour depending on the oxide employed. The ferric-oxide compound of alizarin is violet-black, the chromium-oxide compound claret-colour, the calcium-oxide compound blue, the aluminium-oxide and tin-oxide compounds various shades of red (Turkey-red), and so on.

The method of preparing alizarin indicates it to be a derivative of anthraquinone, but leaves the positions of the hydroxyl-groups indeterminate. The formation of alizarin by heating phthalic anhydride at 150° with catechol and sulphuric acid demonstrates the hydroxyl-groups to be in the same benzene-nucleus; and as those in catechol occupy the *ortho*-position, the same must be true of alizarin:

$$C_6H_4\!<\!\begin{matrix}CO\\CO\end{matrix}\!>\!O + C_6H_4\!<\!\begin{matrix}OH\ ^1\\OH\ ^2\end{matrix} = C_6H_4\!<\!\begin{matrix}CO\\CO\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}OH\ ^1\\OH\ ^2\end{matrix} + H_2O.$$

Phthalic anhydride — Catechol — Alizarin

These facts limit the choice to the two structural formulæ

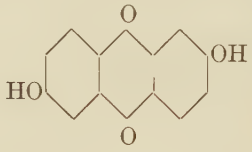
I.  and II. 

The result of nitration indicates formula I to be correct. Two isomeric mononitro-derivatives are obtained, each with the nitro-group in the same nucleus as the hydroxyl-groups, for each can be oxidized to phthalic acid. Formula I alone admits of the formation of two such mononitro-derivatives, and therefore must be correct.

Other hydroxy-derivatives of anthraquinone also are dyestuffs, an example being *purpurin* or 5:6:8-*trihydroxyanthraquinone*,

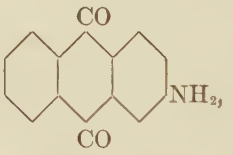
$$C_6H_4{<}(CO)_2{>}C_6H(OH)_3,$$

a constituent of madder-root. The power of the hydroxyanthraquinones to form dyestuffs with mordants is determined by the presence of two hydroxyl-groups in the *ortho*-position to one another, for only under such conditions would the metallic atom of a mordant be able through its secondary valencies to unite with the hydroxyl-groups in producing a ring of five or six members (**374**). A negative proof of the accuracy of this view is afforded by the hydroxyanthraquinones lacking hydroxyl-groups in the *ortho*-position, exemplified by *anthraflavonic acid*,

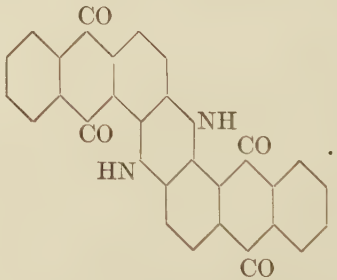


This yellowish-red substance is without dyeing capacity, although it possesses chromophoric carbonyl-groups and tinctophoric auxochromic hydroxyl-groups. Other anthraquinone derivatives with hydroxyl-groups and amino-groups, or with amino-groups only, are also valuable dyestuffs.

The very fast brilliant colours of the *indanthren-group* are derivatives of 2-*aminoanthraquinone*,



being obtained by its oxidation. *Indanthren-blue* is supposed to have the structural formula



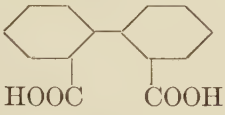
It is prepared by fusing 2-aminoanthraquinone with alkali.

The hydroxyanthraquinones, particularly those having two hydroxyl-groups in the *meta*-position, find application as cathartics.

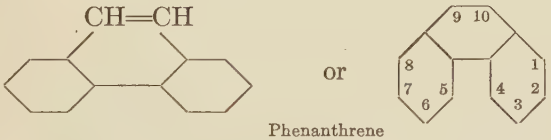
III. PHENANTHRENE, $C_{14}H_{10}$.

386. *Phenanthrene* is isomeric with anthracene, and is present with it in "anthracene-oil." They are separated by the method described in 382. Phenanthrene crystallizes in colourless lustrous plates, soluble in alcohol more readily than anthracene, and yielding a blue fluorescent solution. It melts at 96°, and boils at 340°.

Its oxidation with chromic acid yields *phenanthraquinone*, and then *diphenic acid*,



This reaction indicates phenanthrene to possess two benzene-nuclei in direct union, and therefore to be a diphenyl-derivative, and also a di-*ortho*-compound. Diphenyl with two hydrogen atoms substituted, $-C_6H_4 \cdot C_6H_4-$, or $-C_{12}H_8-$, differs from phenanthrene by C_2H_2. This group must unite two *ortho*-positions, phenanthrene having the constitution



Phenanthrene

This structure finds support in the conversion of stilbene into phenanthrene by passing its vapour through a red-hot tube, a method of formation analogous to that of diphenyl from benzene (371):

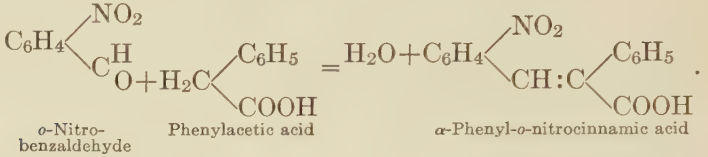
$$\begin{matrix} CH{-}C_6H_5 \\ \| \\ CH{-}C_6H_5 \\ \text{Stilbene} \end{matrix} \quad -H_2 = \quad \begin{matrix} CH{-}C_6H_4 \\ \| \quad | \\ CH{-}C_6H_4 \\ \text{Phenanthrene} \end{matrix} .$$

In the formula of phenanthrene the group —CH=CH— and the four carbon atoms of diphenyl yield a third ring of six carbon atoms. This ring is distinguished from a true benzene-ring by its C_2H_2-group absorbing bromine readily, and by its behaving towards oxidation as an ordinary side-chain.

Phenanthraquinone, $\begin{matrix} C_6H_4{-}CO \\ | \quad | \\ C_6H_4{-}CO \end{matrix}$, is an orange crystalline substance melting at 200°, and boiling without decomposition above 360°. Its diketonic character follows from its yielding di-derivatives with sodium

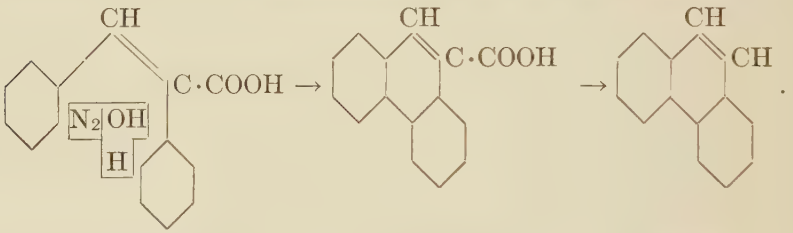
hydrogen sulphite and with hydroxylamine. It is odourless, and is not volatile with steam.

Pschorr discovered an important synthesis of phenanthrene and its derivatives, the condensation of *o*-nitrobenzaldehyde with phenylacetic acid by the Perkin reaction (328):



o-Nitrobenzaldehyde — Phenylacetic acid — *α*-Phenyl-*o*-nitrocinnamic acid

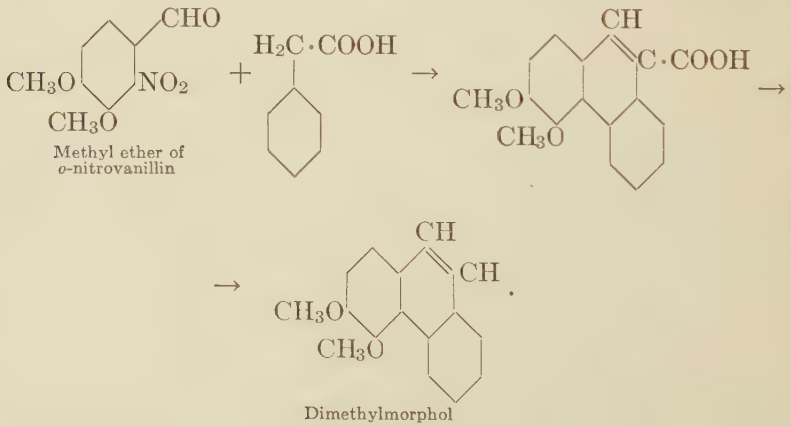
Diazotization of the corresponding amino-acid obtained by reduction, followed by the action of copper-dust (307) on the sulphuric-acid solution of the diazo-compound, eliminates nitrogen and water, an almost quantitative yield of *β-phenanthrenecarboxylic acid* being obtained:



Diazo-derivative of *α*-phenyl-*o*-aminocinnamic acid — Phenanthrene-carboxylic acid — Phenanthrene

Distillation of this acid expels carbon dioxide, forming phenanthrene.

In this reaction, substitution of the methyl ether of o-*nitrovanillin* for *o*-nitrobenzaldehyde gives the dimethoxyphenanthrene *dimethylmorphol*, also formed by the breaking-down of morphine (413):



Methyl ether of *o*-nitrovanillin — Dimethylmorphol

B. HETEROCYCLIC COMPOUNDS.

NUCLEI CONTAINING NITROGEN, OXYGEN, AND SULPHUR.

I. PYRIDINE, C_5H_5N.

387. *Pyridine* and some of its homologues are constituents of coal-tar. Probably they are formed from acetylene and hydrogen cyanide in the manufacture of gas, for the passage of a mixture of these substances through a red-hot tube yields a small proportion of pyridine. On mixing the "Light oil" (283) with sulphuric acid, they are absorbed, and addition of sodium carbonate causes their separation in the form of a dark-brown basic oil. From it pyridine and its homologues are obtained by fractional distillation. Pyridine prepared by this method is never quite pure, but always contains small proportions of its homologues.

Another source of pyridine is "Dippel's oil," a liquid of extremely disagreeable odour, produced by the dry distillation of bones containing their fat. It is a very complex substance, its constituents comprising not only the pyridine bases and quinoline, but also many other substances, such as carbonitriles, amines, and hydrocarbons.

Pyridine is a colourless liquid boiling at 115°, freezing at −38·2°, and with the density 1·0033 at 0°. It is miscible with water in all proportions, and has a weak alkaline reaction, colouring aqueous solutions of litmus only purple. It has a very characteristic odour reminiscent of tobacco-smoke, and is a constituent of crude ammonia. It is very stable, being unattacked by boiling nitric acid or chromic acid. It reacts with sulphuric acid only at high temperatures, yielding a sulphonic acid. The halogens have very slight action on it. Very energetic reduction with hydrogen iodide at 300° yields normal pentane and ammonia.

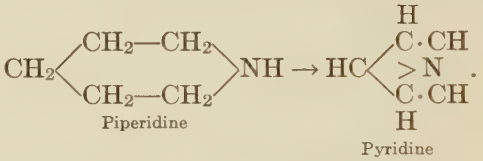
As a base, it forms salts with acids, most of them being readily soluble in water.

Pyridine ferrocyanide dissolves with difficulty, and is employed in the purification of the base. With platinum chloride, the hydrochloride yields

a double salt, $(C_5H_5N)_2H_2PtCl_6$, freely soluble in water. Boiling the solution eliminates two molecules of hydrogen chloride and produces a yellow compound, $(C_5H_5N)_2PtCl_4$, only slightly soluble in water. The reaction affords a sensitive test for pyridine.

The following test also is very delicate. Warming the base with methyl iodide induces an energetic reaction, and forms an addition-product, $C_5H_5N<\overset{CH_3}{\underset{I}{}}$. Heating with solid potassium carbonate causes this compound to emit a very pungent and disagreeable odour.

388. Many methods for the synthesis of pyridine and its homologues are known, although but few of them afford insight into its constitution. Among them is the formation of pyridine from quinoline (400), and that of *piperidine* from 1:5-diaminopentane is mentioned in 159. Piperidine can be oxidized to pyridine by heating it with sulphuric acid:

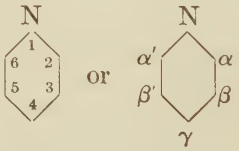


Piperidine — Pyridine

The formation of *β-chloropyridine* from pyrrole is described in 395.

Since under pressure, in presence of colloidal platinum, pyridine in acetic-acid solution is reduced to piperidine almost quantitatively, and piperidine can be oxidized to pyridine, it is reasonable to assume pyridine to have the closed chain characteristic of piperidine, one of five carbon atoms and one nitrogen atom. In addition, the nitrogen atom of pyridine can be proved not to be in union with hydrogen; for, whilst the secondary-amine character of piperidine is indicated by its yielding a nitroso-derivative and by other reactions, pyridine is proved to be a tertiary amine by its yielding an addition-product with methyl iodide (387). The iodine atom in this substance resembles that of the other ammonium iodides in being exchangeable for hydroxyl by means of moist silver oxide.

The number of isomeric substitution-products, like that of benzene (286), indicates *each carbon atom to be in union with one hydrogen atom.* A substance of the formula



should yield three monosubstitution-products, $2(\alpha)=6(\alpha')$, $3(\beta)=5(\beta')$, and $4(\gamma)$. For similar substituents, six disubstitution-products are possible: 2:3=6:5; 3:4=5:4; 2:4=6:4; 2:6, 3:5, and 2:5=6:3. This view agrees with the results of experiment. The mode of union of three out of the four valencies of each carbon atom being established, and that of two of the three nitrogen valencies, it remains only to determine the position in the molecule of the fourth valency of each carbon atom and the third valency of the nitrogen atom.

The marked analogy between benzene and pyridine leads to the assumption of analogous formulæ (287). The great stability of pyridine towards energetic chemical reagents proves its lack of double bonds. Only the side-chains of each compound are attacked by oxidizers. With sulphuric acid, each yields sulphonic acids, convertible by fusion with potassium hydroxide into hydroxyl-derivatives, and by heating with potassium cyanide into cyanides. At 330°, pyridine is converted by a mixture of fuming sulphuric acid and nitric acid into *β-nitropyridine*, colourless needles melting at 41°, and boiling at 216°. The hydroxyl-derivatives of pyridine have the phenolic character, yielding characteristic colorations with ferric chloride. Pyridine therefore must be regarded as benzene with one of its CH-groups replaced by a nitrogen atom.

A remarkable reaction is the introduction of an amino-group into pyridine, effected by Tschitschibabin by dissolving the base in toluene and heating the solution with sodamide. Hydrogen is evolved, and the reaction-product contains the sodium derivative of aminopyridine:

$$C_5H_5N+NaNH_2 \rightarrow C_5H_4N\cdot NHNa+H_2.$$

Decomposition of this product by the action of water gives a good yield of *2-aminopyridine*, a substance melting at 57°. It has been known for a long time, having been prepared by another method.

The analogy between benzene and pyridine also finds expression in the substitution of hydrogen, exemplified by the entrance of the nitro-group and of the sulpho-group at the β-position, and by the fact of a chlorine atom situated at the α-position or the γ-position having greater mobility than one at the β-position. In this respect the ring-nitrogen is comparable with a strongly negative substituent in the benzene-nucleus.

The principle of the orientation of pyridine is similar to that of benzene, conversion of a compound of unknown structure into one

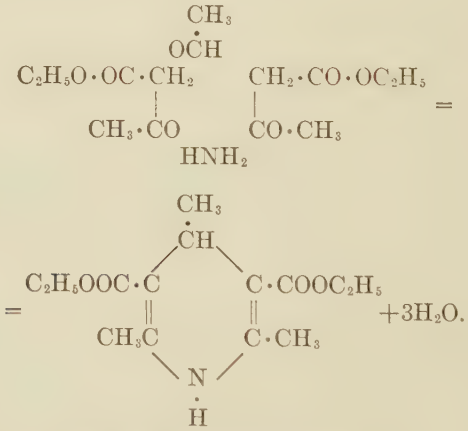
with its side-chains in known positions. The monocarboxylic acids and dicarboxylic acids have served as the main basis for its orientation. The method of ascertaining the positions occupied by the carboxyl-groups in these compounds is described in **391**.

Homologues of Pyridine.

389. The homologues of pyridine are the *methylpyridines* or *picolines*, *dimethylpyridines* or *lutidines*, and *trimethylpyridines* or *collidines*. Many of them can be obtained by more or less complex methods, β-picoline being formed by the distillation of acraldehydeammonia (**141**), and collidine by the distillation of crotonaldehydeammonia. The production of pyridine and its homologues by the dry distillation of bones depends on these reactions. Under the influence of heat, the fat present yields acraldehyde, and it reacts with the ammonia formed by the heating of the proteins to give pyridine bases.

Passage of a mixture of acetylene and ammonia over oxide of aluminium, ferric oxide, or chromium sesquioxide at 300°, yields α-picoline, γ-picoline, and some higher homologues. Owing to the presence of a trace of moisture, acetaldehyde is the initial product, and unites with ammonia to form acetaldehydeammonia.

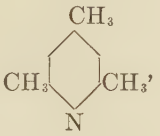
Hantzsch discovered an important synthesis of pyridine derivatives, the condensation of one molecule of acetaldehydeammonia with two molecules of ethyl acetoacetate:



Diethyl dihydrocollidinedicarboxylate

Oxidation of the product with nitrous acid removes two hydrogen atoms, one from the CH-group and one from the imino-group, with formation of *ethyl collidinedicarboxylate*. Saponification of this ester with potassium

hydroxide, and subsequent heating of the potassium salt with quicklime, eliminate the carboxyl-groups, and collidine,



distils.

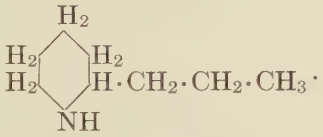
In this synthesis acetaldehyde can be replaced by other aldehydes, and ethyl acetoacetate by the esters of other β-ketonic acids, the method being applicable to the preparation of numerous pyridine derivatives.

Some of the homologues of pyridine can be obtained from it by the action of an alkyl iodide, an addition-product being formed. Heating this compound at 300° detaches the alkyl-group from the nitrogen atom and attaches it to a carbon atom, a reaction analogous to the formation of *p*-toluidine by heating methylaniline hydrochloride at a high temperature (**299**).

390. *α-Propenylpyridine* is of theoretical importance. LADENBURG obtained it by the condensation of α-picoline with acetaldehyde:

$$\underset{\alpha\text{-Picoline}}{NC_5H_4\cdot CH_3} + \underset{\text{Acetaldehyde}}{OCH\cdot CH_3} = \underset{\alpha\text{-Propenylpyridine}}{NC_5H_4\cdot CH{:}CH\cdot CH_3} + H_2O.$$

By its aid he effected the first synthesis of a natural alkaloid, that of *coniine*, $C_8H_{17}N$ (**409**). α-Propenylpyridine was reduced with sodium and boiling alcohol, yielding *α-propylpiperidine*,

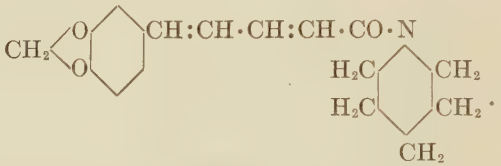


Like all synthetic substances prepared from inactive material, this product is optically inactive. It was resolved into a dextrorotatory and a lævorotatory modification by fractional crystallization of its tartrate, the dextrorotatory isomeride being identical with natural coniine.

The constitutional formula of α-propylpiperidine indicates the carbon atom in union with the propyl-group to be asymmetric. γ-Propylpiperidine does not contain an asymmetric carbon atom,

and therefore should be optically inactive. The side-chain cannot be at the β-position, for coniine is converted into ammonia and normal octane by strong heating with hydrogen iodide. Under similar conditions, a β-propylpiperidine or γ-propylpiperidine must yield an octane with a branched carbon-chain, proving coniine to be an α-compound.

Piperidine is present in pepper in combination as *piperine*, $C_{17}H_{19}O_3N$. Boiling piperine with alkalis yields *piperic acid* (**353**), $C_{12}H_{10}O_4$, and piperidine, the reaction involving the addition of one molecule of water, and indicating piperine to be a substituted amide of piperic acid, containing the piperidine-residue, $C_5H_{10}N$—, instead of the amino-group:

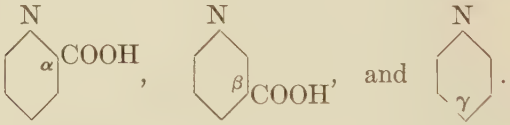


Piperine

Piperidine is a colourless liquid boiling at 106°, with a characteristic pepper-like odour and strongly-marked basic properties (**159**). It is obtained best by the electro-reduction of pyridine.

Pyridinecarboxylic Acids.

391. Three *pyridinemonocarboxylic acids* are known:

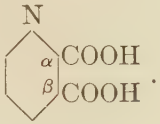


Picolinic acid (α) M.P. 135° | Nicotinic acid (β) M.P. 231° | *iso*Nicotinic acid (γ) M.P. 309°

The orientation of the carboxyl-groups in these acids can be effected as follows. In **390** the side-chain in coniine is stated to occupy the α-position. Oxidation of this substance yields picolinic acid, by conversion of the propyl-group into a carboxyl-group, and elimination of the six added hydrogen atoms. Picolinic acid is therefore the α-carboxylic acid.

The following reasoning establishes the β-constitution of nicotinic acid. Quinoline (**400**) has the formula

being naphthalene with one of the α-CH-groups replaced by nitrogen. Oxidation of quinoline yields a pyridinedicarboxylic acid, *quinolinic acid*, and its structure must be



Heat eliminates from this acid one molecule of carbon dioxide, with formation of nicotinic acid. Since the carboxyl-group in picolinic acid has been proved to occupy the α-position, nicotinic acid must be the β-acid. There remains only the γ-structure for *iso*nicotinic acid.

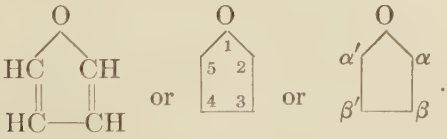
The pyridinemonocarboxylic acids are formed by the oxidation of the homologues of pyridine containing a side-chain. Nicotinic acid derives its name from its formation by the oxidation of nicotine. The monocarboxylic acids are crystalline, and possess both a basic and an acidic character. As bases they yield salts with acids, and they give double salts with such reagents as platinum chloride and mercuric chloride. As acids, they form salts with bases, the copper salts often being employed in their separation.

Picolinic acid can be distinguished from its isomerides by two properties: heating it eliminates carbon dioxide more readily, with formation of pyridine; and it gives a yellowish-red coloration with ferrous sulphate. Quinolinic acid answers the same tests, indicating them to be applicable to acids with a carboxyl-group in the α-position.

II. FURAN, C_4H_4O.

392. *Furan*, C_4H_4O, boils at 36°. It is of little importance, but two of its substitution-products must be considered in some detail.

To furan is assigned the ring-formula



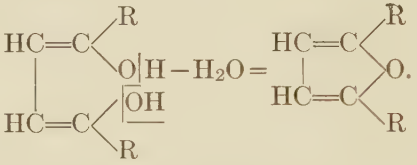
This formula is supported by the resemblance in properties between some of its derivatives, such as *furfural* (*furfuraldehyde*), $C_4H_3O\cdot C\overset{H}{\underset{O}{}}$, and the corresponding benzene derivatives. In addition, the oxygen atom can be proved to be united similarly to that of ethene oxide (150), for with sodium furan does not evolve hydrogen, proving the absence

of a hydroxyl-group; and it does not react with hydroxylamine or phenylhydrazine, indicating the lack of a carbonyl-group.

Furan derivatives can be obtained from the 1:4-diketones, $R\cdot CO\cdot CH_2\cdot CH_2\cdot CO\cdot R$, by means of dehydrators such as acetyl chloride. This reaction can be regarded as consequent on the conversion of the diketone into an unstable tautomeric form,

$$R\cdot\dot{C}(OH):CH\cdot CH:\dot{C}(OH)\cdot R,$$

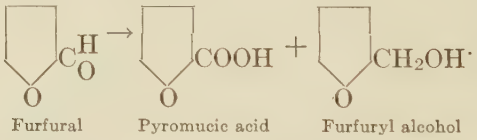
this tautomeride losing water:



This method yields 2:5-furan derivatives, the carbon atoms in furan being denoted as in the formula given. This synthesis of furan derivatives is likewise a proof of their constitution.

393. The most important derivatives of furan are *furfural*, $C_4H_3O\cdot C\overset{H}{\underset{O}{}}$, and *pyromucic acid*, $C_4H_3O\cdot COOH$. Both of them have been known for a long time.

Furfural is prepared from pentoses by the method mentioned in **207**. It has the character of an aromatic aldehyde, resembling benzaldehyde (**314**) in its conversion by alcoholic potassium hydroxide into the corresponding acid, pyromucic acid, and the corresponding alcohol, *furfuryl alcohol*, $C_4H_3O\cdot CH_2OH$:

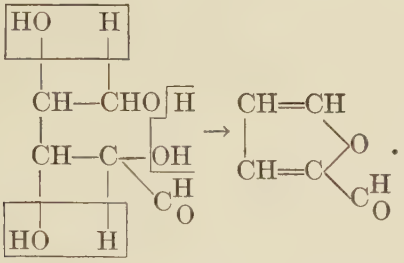


With ammonia it yields *furfuramide*, $(C_5H_4O)_3N_2$, analogous in composition to hydrobenzamide (**315**). As benzaldehyde condenses in presence of potassium cyanide to benzoin (**376**), so furfural under the same conditions yields the similarly constituted *furfuroin*,

$$C_4H_3O\cdot\dot{C}(OH)\cdot CO\cdot C_4H_3O.$$

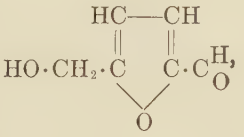
The resemblance in properties between the two compounds is therefore very striking.

Furfural is proved to have the 2-structure by various means, such as its formation from pentoses (**207**), a reaction corresponding with the scheme

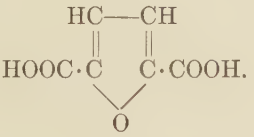


In this process furfural is produced by the elimination of three molecules of water through the influence of hydrogen chloride or sulphuric acid. It is a colourless oily liquid of agreeable colour, and boils at 162°. Two tests for it are described in **207**.

The conversion of pentoses into furfural is analogous to that of ketohexoses into *hydroxymethylfurfural*,



effected by heating with dilute acids. The structure of this substance is indicated by its oxidation to the dibasic *dehydromucic acid*,



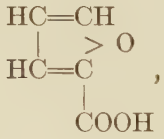
Heating with hydrochloric acid or dilute sulphuric acid converts hydroxymethylfurfural almost quantitatively into formic acid and lævulic acid:

$$\underset{\text{Hydroxymethyl-furfural}}{C_6H_6O_3} + 2H_2O = H\cdot COOH + \underset{\text{Lævulic acid}}{C_5H_8O_3}.$$

The formation of hydroxymethylfurfural is the cause of certain reactions exhibited by the hexoses. When heated with resorcinol and concentrated hydrochloric acid, it yields a dark-red precipitate. This reaction serves to distinguish the artificial honey made from invert-sugar (209) from the natural product, for in the inversion of the sucrose by heating with dilute acid a small proportion of hydroxymethylfurfural is formed.

As indicated by its name, pyromucic acid is formed by the dry distillation of mucic acid (210). It can be obtained also by oxidizing furfural with silver oxide. It is crystalline, melts at 132°, can be sublimed readily, and dissolves freely in hot water. Heating it at its boiling-point, 200°, produces carbon dioxide and furan.

In physical properties pyromucic acid resembles benzoic acid, being readily sublimed, and crystallizing in similar colourless leaflets. In chemical character it resembles the aromatic compounds in a few reactions only, an example being its conversion into a sulphonic acid by means of fuming sulphuric acid. In most of its chemical properties its behaviour approximates more closely to that of an unsaturated aliphatic acid, it being oxidized easily, almost instantaneously decolorizing von Baeyer's reagent (113), and readily adding four bromine atoms. These facts demonstrate the lack of the distinguishing characteristics of the benzene-nucleus, and indicate for it the formula



with two double bonds.

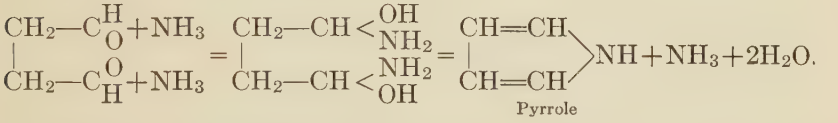
III. PYRROLE, C_4H_5N.

394. Pyrrole is the most important of the heterocyclic compounds with a ring of five atoms. Several natural products containing the pyrrole-nucleus are known, exemplified by the colouring-matter of blood, by chlorophyll, and by such alkaloids as nicotine. Pyrrole derivatives have been found also among the decomposition-products of proteins. Pyrrole is a constituent of "Dippel's oil" (387). The fraction of this oil distilling between 120° and 131° is employed in the preparation of pyrrole. After removal of the pyridine bases by means of dilute sulphuric acid, and of the carbonitriles by boiling with sodium carbonate, the fraction is dried, and brought into contact with potas-

sium. *Potassiopyrrole*, C_4H_4NK, is formed, and can be purified by washing with ether. It is reconverted into pyrrole by the action of water.

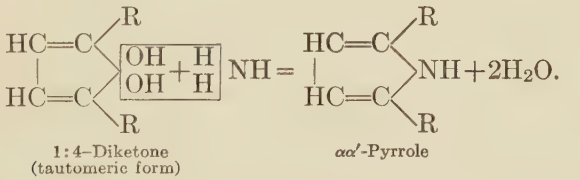
Pyrrole is a colourless liquid insoluble in water. At 20° its density is 0·948, and it boils at 131°. Exposure to light soon imparts to it a brown tint. The vapours of pyrrole and its derivatives colour a wood-shaving moistened with hydrochloric acid carmine red, the effect being due to the formation of the amorphous substance "Pyrrole-red." This reaction furnishes a delicate test for pyrrole and its derivatives.

Pyrrole can be synthesized by several methods, exemplified by the interaction of succindialdehyde and ammonia:

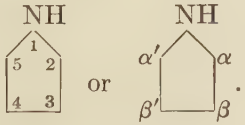


Inversely, *succinald-dioxime* is obtained from pyrrole by the action of hydroxylamine, ammonia being evolved.

The homologues of pyrrole are produced by the interaction of ammonia and 1:4-diketones:



The nomenclature of the pyrrole derivatives is indicated in the scheme



This structure is inferred from the foregoing syntheses and otherwise. The basic properties normally characteristic of a substance with the formula of pyrrole are masked by the resinifying action of acids, sulpho-acids not having been obtained, and nitro-derivatives only by an indirect method.

395. Among the properties of pyrrole indicating its relationship

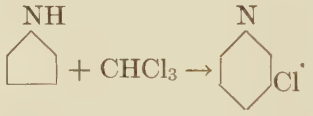
with the aromatic compounds is its behaviour with halogens, for it differs from the aliphatic unsaturated compounds in yielding substitution-products, but not addition-products. The analogy in properties between pyrrole, aniline, and especially phenol, is very marked. The transformation of 1-*methylpyrrole* into 2-*methylpyrrole* under the influence of heat resembles the conversion of methylaniline into *p*-toluidine (**299**):

$$C_4H_4N \cdot CH_3 \rightarrow C_4H_3(CH_3) \cdot NH.$$

1-Methylpyrrole — 2-Methylpyrrole

As sodium phenoxide is converted by carbon dioxide into salicylic acid (**344**), so potassiopyrrole and carbon dioxide yield 2-*pyrrolecarboxylic acid*. Like phenol, pyrrole unites with benzenediazonium chloride, with elimination of hydrogen chloride (**309**).

Contact of pyrrole with chloroform in presence of sodium alkoxide induces a notable reaction. The carbon atom of the chloroform takes up a position between two of the carbon atoms of the pyrrole-nucleus, forming *β-chloropyridine*:



Pyrrole — 3-Chloropyridine

Reduction with zinc-dust and cold hydrochloric acid adds to the pyrrole molecule two hydrogen atoms, and forms 2:3-*dihydropyrrole*, C_4H_7N, boiling at 91°. Like the partial reduction-products of aromatic compounds, dihydropyrrole behaves as an unsaturated compound, another indication of the aromatic character of pyrrole. Further reduction adds two hydrogen atoms, with formation of *tetrahydropyrrole*, C_4H_8NH, the parent substance of proline and hydroxyproline (**252**, 5).

Very important researches on *chlorophyll* have been made by Willstätter and Stoll. This substance is indispensable for the assimilation process, and constitutes between 0·6 and 1·2 per cent. of the weight of dried leaves. Its molecule contains magnesium in complex combination. Towards alkalis the magnesium-complex is very stable, but the metal is eliminated readily from the molecule by means of acids.

Chlorophyll is saponified by alkali-metal hydroxides, with formation of the unsaturated alcohol *phytol*, $C_{20}H_{39}OH$. During the reaction the alkali combines with polybasic acids, the *chlorophyllins*, substances con-

vertible into an oxygen-free product, *aetiophyllin*, $C_{31}H_{34}N_4Mg$, by elimination of the carboxyl-groups. Acids replace the magnesium atom in this compound by two hydrogen atoms, forming *aetioporphorin*, $C_{31}H_{36}N_4$. This derivative can be obtained also from hæmin (250), an indication of the relationship of chlorophyll and hæmoglobin, the colouring matter of blood. Hæmin contains iron instead of magnesium.

Reduction of aetioporphorin yields a mixture of pyrrole homologues, each nitrogen atom being associated with a pyrrole-nucleus.

The chlorophyll of all plants is identical, and consists of a mixture of two related compounds, chlorophyll-*a* and chlorophyll-*b*, there being about one molecule of *b* to three molecules of *a*. Their formulae are

a. $C_{55}H_{72}O_5N_4Mg = (MgN_4C_{32}H_{30}O)\begin{cases}COOCH_3\\COOC_{20}H_{39}\end{cases}$, and

b. $C_{55}H_{70}O_6N_4Mg = (MgN_4C_{32}H_{28}O_2)\begin{cases}COOCH_3\\COOC_{20}H_{39}\end{cases}$.

IV. THIOPHEN, C_4H_4S.

396. *Thiophen* has a more aromatic character than furan or pyrrole. It is present to the extent of about 0·5 per cent. in the crude benzene obtained from coal-tar (283). Its homologues, *thiotolen* or methylthiophen, and *thioxen* or dimethylthiophen, are contained in toluene and xylene from the same source.

Thiophen was obtained originally by Victor Meyer by agitating coal-tar benzene with small proportions of concentrated sulphuric acid until it ceased to give the *indophenin-reaction*, a blue coloration with isatin (403) and concentrated sulphuric acid containing a trace of nitric acid. The thiophen becomes converted into a sulphonic acid, and can be regenerated by the action of superheated steam.

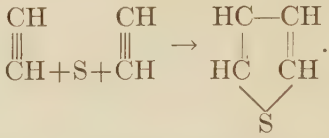
A better method for the separation of benzene and thiophen is to boil the crude benzene with mercuric oxide and acetic acid. The thiophen is precipitated as *thiophen mercury oxyacetate*,

$$C_4H_2S(HgOOC\cdot CH_3)\cdot HgOH,$$

a substance reconvertible into thiophen by distillation with hydrochloric acid of moderate concentration. It is formed by passing acetylene over pyrites at 300°.

Thiophen can be synthesized by various methods. The interaction

of acetylene and iron pyrites, FeS_2, at about 300° yields a liquid containing fifty per cent. of thiophen:

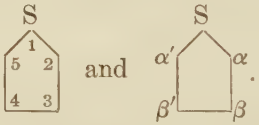


Heating sodium succinate with phosphorus pentasulphide induces a vigorous reaction, attended by the evolution of carbon disulphide and the distillation of a liquid consisting mainly of thiophen.

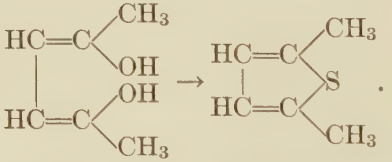
It is a colourless liquid boiling at 84°, a temperature near to the boiling-point of benzene (80·4°). It has a faint, non-characteristic odour. It is heavier than water, its density at 23° being 1·062.

Bromine reacts energetically with thiophen, forming chiefly *dibromothiophen*, $C_4H_2Br_2S$, with a small proportion of the monobromo-derivative.

The notation of thiophen derivatives is indicated by the schemes

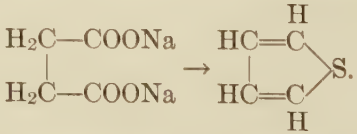


The homologues of thiophen can be obtained by the WURTZ-FITTIG synthesis (**284**) and by other methods, such as heating 1:4-diketones with phosphorus pentasulphide, a mode of synthesis indicating the constitution of the thiophen homologues. By this process acetonylacetone yields *dimethylthiophen*:



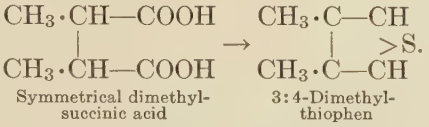
Acetonylacetone (tautomeric form) — 2:5-Dimethylthiophen

2:5-Dialkylthiophens are obtained from 1:4-diketones, and the 3:4-alkyl-compounds can be prepared by another method. As stated, thiophen is produced by the interaction of sodium succinate and phosphorus pentasulphide:



Sodium succinate — Thiophen

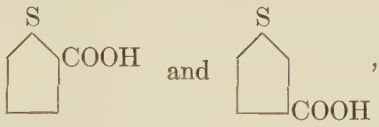
The conversion of a monoalkylsuccinic acid into a 3-alkylthiophen, and that of a symmetrical dialkylsuccinic acid into a 3:4-alkylthiophen, are analogous:



Symmetrical dimethylsuccinic acid — 3:4-Dimethylthiophen

The known structure of these compounds can be employed as a basis for the orientation of the derivatives of thiophen.

397. When a cold aqueous solution of the two monocarboxylic acids, 2-*thiophencarboxylic acid* and 3-*thiophencarboxylic acid*,



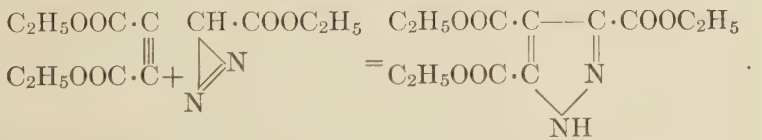
is crystallized slowly, the mixture formed cannot be resolved into its components. This phenomenon is due to the formation of mixed crystals, and is of rare occurrence with position-isomerides.

A *thiophensulphonic acid* also is known. It is produced more easily than benzenesulphonic acid, a fact constituting the basis of Victor Meyer's method of separating thiophen and benzene.

A mixture of acetic anhydride and concentrated nitric acid reacts with thiophen to form *mononitrothiophen*. It is a solid melting at 44°, and boiling at 224°, and it has an odour like that of nitrobenzene. Its reduction yields *aminothiophen* or *thiophenine*, a substance distinguished from aniline by its instability. It changes quickly to a varnish-like mass, but its hydrochloride is stable. It does not yield diazo-compounds, but reacts with benzenediazonium chloride to form a crystalline orange dyestuff.

V. PYRAZOLE, $C_3H_4N_2$.

398. *Pyrazole derivatives* are produced by the interaction of the esters of unsaturated acids and ethyl diazoacetate. An example is the union with explosive energy of diethyl acetylenedicarboxylate and ethyl diazoacetate to form *triethyl pyrazoletricarboxylate*:

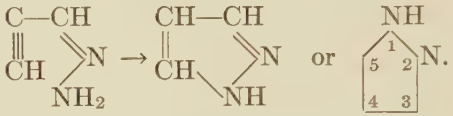


Diethyl acetylenedicarboxylate — Triethyl pyrazoletricarboxylate

Pyrazole is produced by several reactions, one of them being the combination of hydrazine with propiolaldehydeacetal (**142**):

$$CH{\equiv}C\cdot CH(OC_2H_5)_2 + H_2N\cdot NH_2 = CH{\equiv}C\cdot CH{=}N\cdot NH_2 + 2C_2H_5OH;$$

Propiolaldehydeacetal — Intermediate product (not isolated)



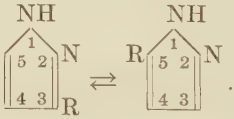
Intermediate product — Pyrazole

This synthesis proves pyrazole to have the formula indicated, and to be pyrrole with one of the CH-groups replaced by a nitrogen atom.

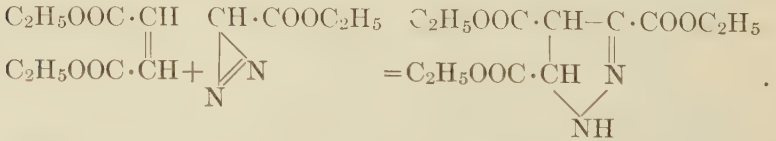
It is crystalline, melts at 70°, boils at 185°, and is very stable. It is only a weak base, for its aqueous solution has a neutral reaction.

Pyrazole has a much more aromatic character than pyrrole. It is very stable towards oxidation, and can be sulphonated and nitrated like benzene. The halogen atom in its monohalogen derivatives can be eliminated only with great difficulty.

The identity of the 3-derivatives and the 5-derivatives of pyrazole is of theoretical interest, for the structural formula given indicates their dissimilarity. After replacement of the hydrogen atom of the imino-group by alkyl or phenyl, the derivatives with substituents at positions 3 and 5 cease to be identical. As migration of the hydrogen atom from one nitrogen atom to the other, with a simultaneous migration of the double bonds, makes position 3 equivalent to position 5, free pyrazole must be assumed to undergo this type of tautomerization readily:

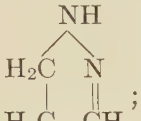


399. The derivatives of pyrazole are not important, but there are valuable products related to its dihydride, *pyrazoline*, $C_3H_6N_2$. Substances of this type are prepared by condensing ethyl diazoacetate with esters containing a double bond:

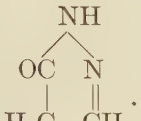


Diethyl fumarate — Triethyl pyrazolinetricarboxylate

Pyrazoline (I) is formed by the interaction of hydrazine hydrate and acraldehyde. Bromine converts it into pyrazole. *Pyrazolone* (II) is a ketonic derivative of pyrazoline:

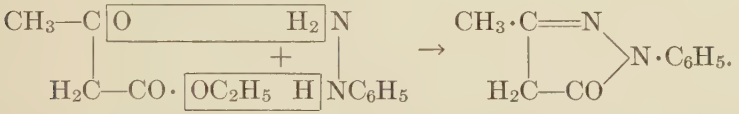


I.

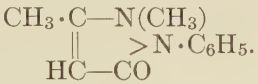


II.

Substitution-products of pyrazolone are obtained by the interaction of ethyl acetoacetate and phenylhydrazine:



Methylphenylpyrazolone is formed by this condensation. A similar process converts methylphenylhydrazine, $C_6H_5 \cdot NH \cdot NH \cdot CH_3$, and ethyl acetoacetate into a dimethylphenylpyrazolone of the formula



This substance is termed "antipyrine," and was discovered by Knorr. It is employed extensively in medicine as a febrifuge. It crystallizes in white leaflets melting at 113°. It cannot be distilled without undergoing decomposition. It is readily soluble in water and alcohol, the aqueous solution giving a red coloration with ferric chloride, and a bluish-green coloration with nitrous acid.

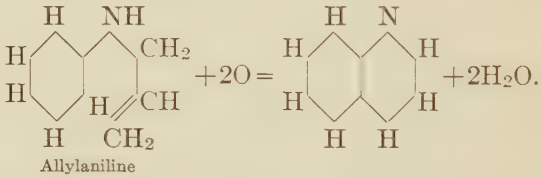
"Salipyrine" is a compound of "antipyrine" and salicylic acid.

CONDENSATION-PRODUCTS OF BENZENE AND HETEROCYCLIC NUCLEI.

I. QUINOLINE, C_9H_7N.

400. Quinoline is present in coal-tar and bone-oil, but is difficult to obtain pure from these sources. It is prepared by SKRAUP's synthesis, described below. It is a colourless, highly refractive liquid of characteristic odour, freezes at $-22{\cdot}6°$, boils at 236°, and at 0° has the density 1·1081. It has the character of a tertiary base, not possessing any hydrogen in union with nitrogen. It yields salts with acids, the dichromate, $(C_9H_7N)_2H_2Cr_2O_7$, dissolving in water with difficulty.

Quinoline can be synthesized by various methods indicating its constitution. Its synthesis was effected first by KÖNIGS, by passing allylaniline-vapour over red-hot oxide of lead:



Allylaniline

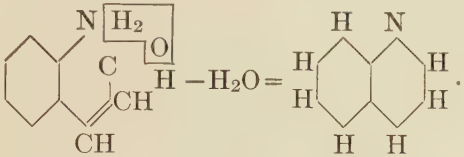
SKRAUP's synthesis consists in heating a mixture of aniline, glycerol, sulphuric acid, and nitrobenzene. In presence of sulphuric acid as a dehydrator, the glycerol loses water and forms acraldehyde, that substance uniting with the aniline to form an addition-product,

$$C_6H_5{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}C\overset{H}{\underset{O}{}}.$$

In KÖNIGS's synthesis the oxidizer is the lead oxide; in this reaction it is the nitrobenzene, it becoming reduced to aniline. Arsenic acid can be substituted for nitrobenzene.

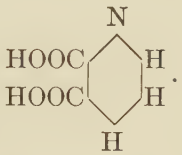
VON BAEYER and DREWSEN discovered another method of synthesis indicating the constitution of quinoline, and involving the reduction of *o*-nitrocinnamaldehyde. This compound becomes converted initially into the corresponding amino-derivative, the hydrogen atoms of the

amino-group of this substance being eliminated subsequently along with the oxygen atom of the aldehyde-group:



o-Aminocinnamaldehyde Quinoline

The last synthesis indicates quinoline to be an *ortho*-substituted benzene, but leaves undetermined the constitution of the ring containing the nitrogen atom. The method employed for its investigation is based on oxidation to the dibasic acid *quinolinic acid*,



Distillation with quicklime converts quinolinic acid into pyridine. These facts indicate quinoline to contain a benzene-nucleus and a pyridine-nucleus, with two *ortho*-carbon atoms common to both. It may be regarded as naphthalene with the CH-group at 1 or 4 or 5 or 8 replaced by nitrogen.

The number of isomeric substitution-products is very large. The seven hydrogen atoms occupy dissimilar positions relative to the nitrogen atom, and consequently seven monosubstitution-products are possible. Twenty-one disubstitution-products are possible for similar substituents, whilst the number of the tri-derivatives possible, and that of the higher derivatives, are much greater.

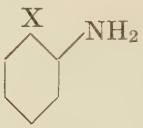
401. There are three methods for the orientation of quinoline derivatives:

First, the relative method (**354**, 1).

Second, oxidation. Usually this process removes the benzene-nucleus, leaving the pyridine-nucleus intact, thereby furnishing a means of identifying the substituents present in each.

Third, SKRAUP'S synthesis. This process is an important aid to orientation. It is applicable not only to aniline, but to many of its substitution-products, such as its homologues, the nitroanilines, the aminophenols, and other derivatives. The quinoline compounds obtained have their substituents in the benzene-nucleus. In addition, this synthesis indicates the positions entered by the side-chains in

reactions employing an *ortho*-substituted aniline or a *para*-substituted aniline:



Ortho

can yield only

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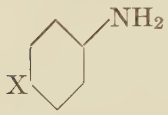
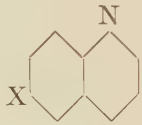
and 

Para

only 

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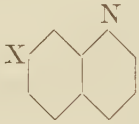
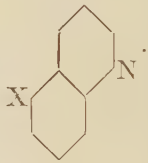
whilst

Meta

can yield 

or 

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Obviously, each of the four possible quinoline derivatives with substituents in the benzene-nucleus can be prepared by SKRAUP's synthesis.

The nomenclature of the quinoline derivatives is indicated in the scheme

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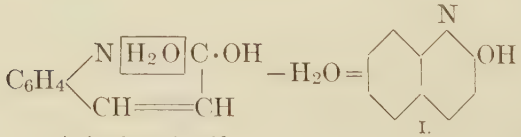
Many of the known quinoline derivatives are obtained by SKRAUP's method, a smaller number directly from quinoline. The sulphonic acids are prepared best by the second method. Fusion with potassium hydroxide converts them into hydroxyquinolines; and heating them with potassium cyanide gives cyanoquinolines, hydrolyzable to carboxylic acids.

Carbostyril or 2-*hydroxyquinoline* can be synthesized by the elimination of water from *o*-aminocinnamic acid:



o-Aminocinnamic acid

Carbostyril

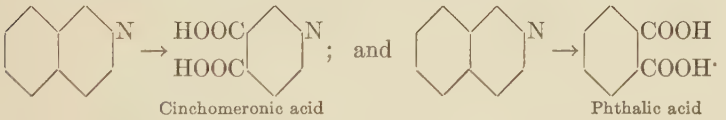
Formula II must be ascribed to the free compound, for its absorption-curve in the ultraviolet region almost coincides with that of a derivative methylated at the nitrogen atom (337). As carbostyril also has phenolic properties, being soluble in alkalis, and being reprecipitated from alkaline solution by carbon dioxide, it is susceptible of transformation into the tautomeric form I.

II. *iso*QUINOLINE, C_9H_7N.

402. iso*Quinoline* is present in coal-tar, and HOOGEWERFF and VAN DORP isolated it from that material in the form of its sparingly soluble sulphate. It is a colourless substance with an odour like that of quinoline. It melts at 21°, and boils at 237°. It has the formula

*iso*Quinoline

This constitution is indicated by its oxidation to *cinchomeronic acid* and phthalic acid, in accordance with the scheme



Cinchomeronic acid Phthalic acid

The synthesis of *iso*quinoline furnishes additional confirmation of the structure indicated.

III. INDOLE, C_8H_7N.

403. The relationship of *indigo* and *indole* is made evident by the following series of transformations, chiefly the discoveries of VON BAEYER.

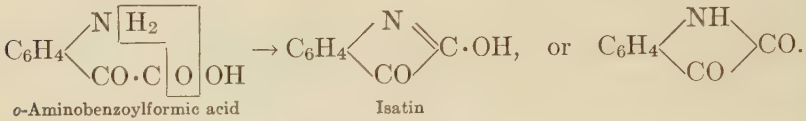
With nitric acid indigo, $C_{16}H_{10}O_2N_2$, yields the oxidation-product *isatin*, $C_8H_5O_2N$, also synthesizable by the action of *o*-nitrobenzoyl chloride on silver cyanide. Hydrolysis of the carbonitrile produced gives *o*-nitrobenzoylformic acid:

$$C_6H_4{<}\begin{matrix}NO_2\\CO\cdot Cl\end{matrix}\ ^{1}_{2} \rightarrow C_6H_4{<}\begin{matrix}NO_2\\CO\cdot CN\end{matrix} \rightarrow C_6H_4{<}\begin{matrix}NO_2\\CO\cdot COOH.\end{matrix}$$

o-Nitrobenzoyl chloride — *o*-Nitrobenzoyl cyanide — *o*-Nitrobenzoyl-formic acid

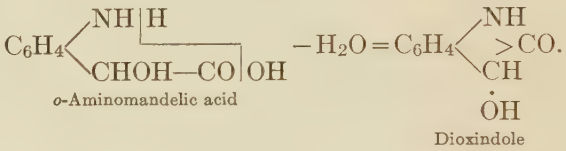
Reduction converts the nitro-group in this acid into an amino-group, and simultaneously eliminates water with the formation of

isatin, indicating the constitution of this derivative to be that given in the scheme



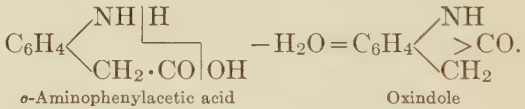
o-Aminobenzoylformic acid — Isatin

Through reduction with zinc-dust and hydrochloric acid, isatin adds two hydrogen atoms, forming *dioxindole*, $C_8H_7O_2N$. This compound is produced also by the elimination of water from the unstable *o*-aminomandelic acid, a reaction indicating its constitution:



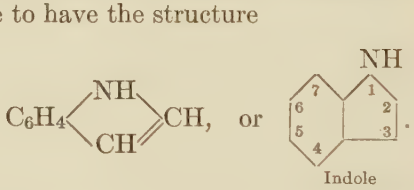
o-Aminomandelic acid — Dioxindole

The reduction of dioxindole by tin and hydrochloric acid gives *oxindole*, C_8H_7ON, also obtainable by the reduction of *o*-nitrophenylacetic acid and subsequent elimination of water:



o-Aminophenylacetic acid — Oxindole

Distillation with zinc-dust converts oxindole into *indole*, C_8H_7N, indicating indole to have the structure



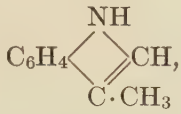
Indole

Indole therefore possesses a benzene-nucleus condensed with a pyrrole-nucleus. It displays some of the properties characteristic of pyrrole, being a very weak base, and giving a red coloration with hydrogen chloride.

Indole is present in small proportion in coal-tar and in oil of jessamine. It can be isolated as potassium derivative with the metal in union with nitrogen by heating with potassium hydroxide the coal-tar fraction boiling between 240° and 260°. In spite of its characteristic and disagreeable odour, it is employed in the manufacture of perfumes. It

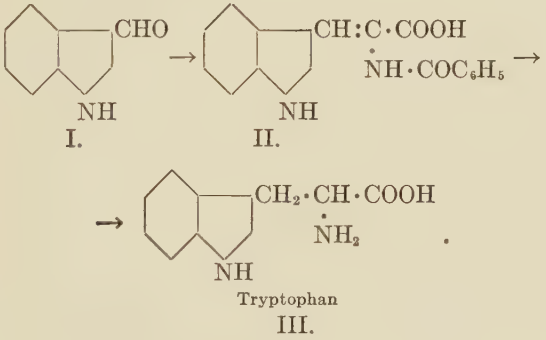
forms white leaflets melting at 52°, and is readily volatile with steam. Its picrate crystallizes in well-developed red needles.

3-*Methylindole* or *scatole*,



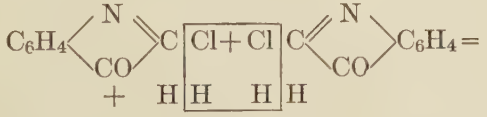
is present in fæces, and occasions the unpleasant odour. It is found also in a species of wood grown in India, and is formed in the putrefactive decay of proteins, or by fusing them with potassium hydroxide.

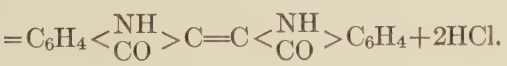
Tryptophan or *indolealanine*, $C_{11}H_{12}O_2N_2$, melts at 289°. It is an important decomposition-product of proteins (**252**, 5) and an indole derivative. It is synthesized from indole by the action of chloroform and potassium hydroxide in alcoholic solution. 3-*Indolealdehyde* (I) is formed as an intermediate product, and with hippuric acid condenses to *indolylbenzoylaminoacrylic acid* (II). Under the influence of sodium and alcohol, the double bond of this compound adds two hydrogen atoms and the benzoylgroup is eliminated simultaneously, with formation of racemic tryptophan (III):



Indigo.

404. The constitution of *indigo* is inferred from its formation from *isatin chloride*, obtained by the interaction of isatin and phosphorus pentachloride. Reduction of isatin chloride by zinc-dust and acetic acid transforms it into indigo:





As the action of sulphuric acid and subsequent reduction converts *di-(o-nitrophenyl)-diacetylene*, $\begin{matrix} C_6H_4\cdot C\equiv C-C\equiv C\cdot C_6H_4 \\ \cdot \qquad\qquad\qquad\qquad \cdot \\ NO_2 \qquad\qquad\qquad NO_2 \end{matrix}$, into indigo, the two isatin-residues in indigo must be united by a carbon valency.

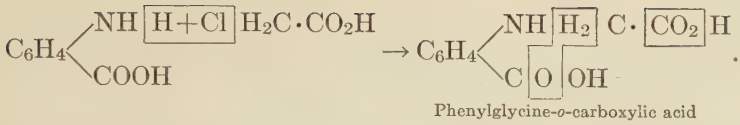
Indigo has been known for a long time as one of the best blue dyestuffs. It is very fast, and is unaffected by light, acids, alkalis, or washing. It can be prepared from certain plants, among them *Indigofera sumatrana* and *I. arrecta*. Formerly these plants were cultivated extensively in Bengal in India, the origin of the name of the dyestuff, and also in Java, China, Japan, and South America. Since its introduction, synthetic indigo (405) has displaced the natural product to a very great extent, even in these countries, and the competition became so keen as to lead to the abandonment of many indigo-plantations, and the financial ruin of their proprietors. The indigo in the plant is not in the free state, but exists chiefly in the leaves in combination as the glucoside *indican*, a crystalline substance extractable with hot water, and having the formula $C_{14}H_{17}O_6N,3H_2O$. In addition to the glucoside, the leaves contain an enzyme, its activity resembling that of all enzymes in being destroyed by boiling water. In preparing indican itself, it is necessary to extract with water at that temperature. Cold water dissolves both the indican and the unchanged enzyme, and the glucoside decomposes into dextrose and *indoxyl*, C_8H_7ON or

$$C_6H_4\left\langle\begin{matrix} NH \\ C(OH) \end{matrix}\right\rangle CH,$$

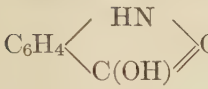
a substance moderately stable in acid solution, but in dilute alkaline solution quickly oxidized to indigo by atmospheric oxygen.

Indigotin is a dark-blue powder, a copper-like lustre being developed by milling. It can be sublimed *in vacuo*, enabling its vapour-density to be determined. It is insoluble in most solvents, but can be crystallized from nitrobenzene and from aniline. It dissolves in fuming sulphuric acid to form sulphonic acids.

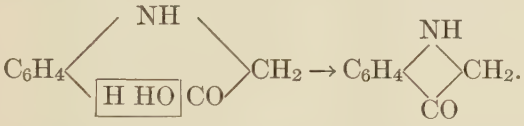
405. The great industrial importance of indigo has induced many attempts to synthesize it. One method is a commercial success, and enables the artificial product to be sold at a much lower price than that formerly obtained for natural indigo. It yields pure indigotin, an additional advantage. Anthranilic acid or *o*-aminobenzoic acid (347), $C_6H_4<\begin{matrix} NH_2 \\ COOH \end{matrix}$, combines with monochloroacetic acid to form *phenylglycine-o-carboxylic acid*:



Phenylglycine-*o*-carboxylic acid

Fusion with sodium hydroxide transforms this acid into indoxyl,  , the product in alkaline solution becoming converted by atmospheric oxidation into indigo.

Another process involves the interaction of aniline and monochloroacetic acid to form *phenylglycine*, $C_6H_5 \cdot NH \cdot CH_2 \cdot COOH$, convertible into indoxyl by fusion with sodamide, NH_2Na:



Tautomeric form of indoxyl

The reduction of indigo in alkaline solution adds two hydrogen atoms, with formation of *indigo-white*, $C_{16}H_{12}O_2N_2$. It is a white crystalline substance, its phenolic character being indicated by its solubility in alkalis. In alkaline solution it is reconverted rapidly into indigo by atmospheric oxidation, a reaction employed in dyeing with this substance. The dyestuff is reduced first to indigo-white, and the fabric is soaked thoroughly in an alkaline solution of that compound, subsequent exposure to air developing the indigo-blue on the fibres. The process is known technically as "indigo vat-dyeing."

The mode of reduction of indigo to indigo-white in the dyeing-industry depends on whether wool, silk, or cotton is to be dyed. For wool and silk the best reducer is a salt of hydrosulphurous acid, $H_2S_2O_4$, ("Inorganic Chemistry," 82) or "rongalite" (108). The solution is mixed with zinc hydrosulphite, and excess of milk of lime is added, zinc hydroxide being precipitated. The indigo is mixed with water, and warmed at about 60° with the solution of calcium hydrosulphite, a concentrated alkaline solution of indigo-white being obtained in a short time. The addition of sufficient water to the solution in the dyeing-vat completes the preparation of the bath.

An advantage of the hydrosulphite reduction-process is the limitation of the reduction to the formation of indigo-white, very little of the indigo being lost.

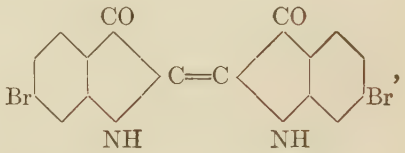
Indigo is the oldest and most important member of the series of *vat-dyestuffs*. They include pigments insoluble in water, but characterized by

their ready reduction to a form soluble in dilute alkali, by their affinity in this condition for vegetable and animal fibres, and by their subsequent reoxidation on the fibre to the original insoluble condition.

The vat-method of dyeing has great advantages over other processes, the fabric not requiring preliminary mordanting, and both the preparation of the bath and the operation of dyeing usually being effected at the ordinary temperature. A further advantage is the very fast nature of the colours imparted by these dyestuffs.

Vat-dyestuffs derived from indigo, and others related to anthraquinone, are known. Those of the first type are the *indigoids*, and contain the chromophoric group —CO·C:C·CO—.

Substitution by halogen of the hydrogen atoms in the benzene-nuclei of indigo produces a marked change in colour only after replacement of the hydrogen atoms occupying the *para*-positions to the carbonyl-groups. *Symmetrical dibromoindigo,*



is the celebrated "Purple of the ancients" employed in antiquity for dyeing Tyrian purple. Formerly it was obtained from the colour-yielding glands of the mollusc *Murex brandaris* in the form of a colourless substance converted into the dyestuff by the action of light.

Thioindigo is a reddish-blue derivative with two sulphur atoms replacing the two imino-groups. The tint of the dyestuff can be altered by substitution so as to render possible the production of almost every shade.

ALKALOIDS.

406. Plants of certain families contain substances termed *alkaloids*, usually of complex composition and basic character. Their classification in one group is of old standing, and had its origin in a conception similar to that accepted for the vegetable acids (1) prior to the determination of their constitution. These acids have been subdivided into such different types as monobasic, polybasic, aliphatic, and aromatic acids; and the individual alkaloids can be arranged similarly in different classes. Most of the alkaloids are related to pyridine, quinoline, or *iso*quinoline, whilst a smaller number belongs to the aliphatic series. Some of the aliphatic members are described with the compounds of similar chemical character. Among them are betaine (242); choline (160); caffeine; and theobromine (272). Only alkaloid derivatives of pyridine are described in this chapter, the name alkaloids in its more restricted sense being applied to them. The other substances are known as vegetable bases.

PROPERTIES.

407. Only a few alkaloids, such as *coniine* and *nicotine*, are liquids, most of them being crystalline. Many are optically active and lævorotatory, it being very exceptional for them to exhibit dextrorotation. They have an alkaline reaction and a bitter taste. Most of them are insoluble in water, more or less soluble in ether, and readily soluble in alcohol. Most alkaloids are insoluble in alkalis, but dissolve in acids to form salts, some of the products being well-defined crystalline substances.

Some compounds precipitate many of the alkaloids from aqueous or acidic solution. Examples of such *general alkaloid-reagents* are tannin (347), phosphomolybdic acid, and mercuric potassium iodide, KI,HgI_2 ("Inorganic Chemistry," 283). Some alkaloids are excessively poisonous.

> Strong tea can be employed sometimes as an antidote, the tannin precipitating the alkaloid and rendering it innocuous.

Some of the alkaloids, such as quinine and strychnine, give very characteristic colour-reactions. Despite the obscure nature of these processes, they afford a reliable means of detecting even small quantities of such alkaloids.

The complex structure of many alkaloids renders their investigation a matter of extreme difficulty, and despite a century of unremitting toil the elucidation of the constitution of all these substances is far from attainment. The research involves the identification of the well-known groups present in the molecule, such as OH, OCH_3, C=C, CO, and CH_3; and also includes the determination of the particular ring of the carbon-nitrogen-nucleus in union with these groups.

Study of the first problem has demonstrated most alkaloids to be tertiary amines yielding addition-products with methyl iodide. Many alkaloids contain acid-residues or methoxyl-groups, $—OCH_3$. The acid-residues can be eliminated by saponification with hot bases or acids; and the methoxyl-groups can be removed as methyl iodide by Zeisel's method of heating with hydrogen iodide (220). Hydroxyl-groups can be detected in the ordinary way by means of acid chlorides or acetic anhydride.

The investigation of the nucleus involves an attempt to break it down, good results sometimes having been obtained with powerful oxidizers such as potassium permanganate, chromic anhydride, and nitric acid. Distillation with zinc-dust and fusion with potassium hydroxide have been of service also.

The alkaloids are present throughout the whole vegetable kingdom, but their distribution among the various plant families is very uneven. They are found chiefly in the dicotyledonous plants, certain orders of this class, such as *Papaveraceæ*, *Solanaceæ*, and *Ranunculaceæ*, containing alkaloids in great abundance. Alkaloidal plants seldom have only a single alkaloid, but those occurring together in one plant are generally closely related in structure. Alkaloids are found in all the parts of plants, but occur chiefly in the tissues of vigorous growth, spreading thence to the rest of the plant and accumulating there. They never exist in the free state in the plants, but in union with acids such as oxalic acid, malic acid, succinic acid, and others.

In the extraction of the alkaloids from plants the material is cut into fine pieces and lixiviated with acidified water in a conical vat tapering towards the bottom, and having at that position a layer of some material such as glass-wool or lint. The effect is to cause the acidified water to sink gradually through a thick layer of the substance under extraction, a process technically known as "Percolation." Dye-stuffs, carbohydrates, inorganic salts, etc., are dissolved with the alkaloids. An alkaloid volatile with steam can be separated by this means from the liquid, provided the mixture has been rendered alkaline. A comparatively insoluble alkaloid can be obtained by filtration.

Further purification is always necessary, and is effected by crystallizing the free alkaloid or one of its salts several times.

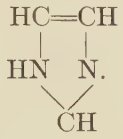
408. Constitution furnishes the best basis for the classification of the alkaloids. PICTET recognizes eleven groups:

I. **Aliphatic Bases.** Methylamine, choline, betaine, and muscarine (present in toad-stool, *Agaricus muscarius*).

II. **Tetrahydropyrrole Bases** (395). Tetrahydropyrrole, C_4H_9N, has been detected in tobacco and opium.

III. **Pyridine Derivatives.** Piperine (390), and coniine (409).

IV. **Iminazole Derivatives.** Iminazole has the formula



This class includes allantoine (271), a constituent of sugar-beet and of other substances.

V. **Alkaloids with Condensed Tetrahydropyrrole and Piperidine Chains.** Atropine, and cocaine.

VI. **Purine Derivatives.** Xanthine, caffeine, and theobromine.

VII. **Aromatic Amines.** Hordenine, and tyramine.

VIII. **Indole Derivatives.** Strychnine.

IX. **Quinoline Derivatives.** Quinine.

X. ***iso*Quinoline Derivatives.** Morphine, and narcotine.

XI. **Alkaloids of Unknown Structure.** Aconitine, colchicine, cytisine, and so on.

INDIVIDUAL ALKALOIDS.

Coniine, $C_8H_{17}N$.

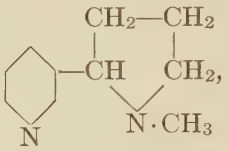
409. The synthesis of *coniine* is described in 390. It is present in spotted hemlock (*Conium maculatum*), and is a colourless liquid of stupefying odour. It boils at 167°, is but slightly soluble in water, and is very poisonous.

Nicotine, $C_{10}H_{14}N_2$.

410. *Nicotine* is present in combination with malic acid and citric acid in the leaves of the tobacco-plant (*Nicotiana tabacum*). It is a colourless, oily, lævorotatory liquid. It has a tobacco-like odour, but the smell is not so marked in a freshly-distilled sample as it becomes later. Nicotine boils at 246·7°, and is excessively poisonous. It turns brown quickly in the air. It is a ditertiary base. Oxidation with

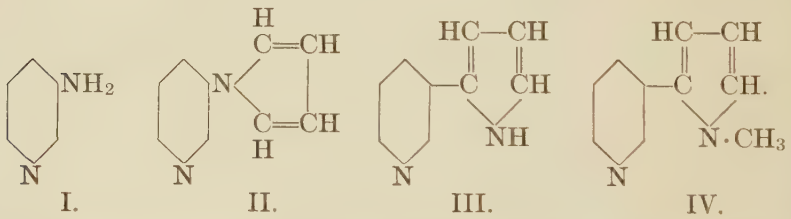
potassium permanganate converts it into nicotinic acid (**391**), indicating it to be a β-derivative of pyridine.

The constitutional formula of nicotine is



with a hydrogenated pyrrole-nucleus methylated at the nitrogen atom, and a β-substituted pyridine-nucleus. The formula also indicates nicotine to be a ditertiary base, and to be oxidizable to nicotinic acid.

Evidence in favour of this formula is furnished by PICTET'S synthesis, the starting point being 3-*aminopyridine* (I), its mucate being convertible by heat into N-(3-*pyridyl*)-*pyrrole* (II) (**394**). Heating transforms this nitrogen-substituted pyrrole derivative into a carbon-substituted pyrrole (III); and the action of methyl iodide changes the potassium compound of this substance into *nicotyrine* (IV), a product with four hydrogen atoms less than nicotine. Prior to its synthesis by this method nicotyrine had been prepared by the oxidation of nicotine with silver oxide. Nicotyrine can also be produced very readily by passing nicotine vapour over finely-divided platinum at 320°, two molecules of hydrogen being eliminated:



I. II. III. IV.

The pyrrole-nucleus of nicotyrine can be reduced by a circuitous way to a tetrahydropyrrole-nucleus, an optically inactive nicotine being formed. The lævorotatory isomeride is identical with natural nicotine. The dextrorotatory form is much less poisonous than the lævorotatory modification, and also differs from it in other physiological actions.

Nicotine dissolves in its own volume of water to form a sticky viscous liquid resembling glycerol. Warming renders this liquid turbid, and separates it into two liquid layers, the upper being a saturated solution of nicotine in water, and the lower a saturated solution of water in nicotine.

Systematic investigation of mixtures of nicotine and water in various proportions and at various temperatures has proved the two liquids to be

miscible in all proportions below 60° and above 208°. For this range of temperature the mutual solubility is limited. A graphic representation of the solubilities (Fig. 79) gives a closed curve. The region inside this curve corresponds with two liquid layers, that outside the curve with miscibility in all proportions.

The addition of nicotine to water at 90° is followed initially by complete solution. At a concentration of about 6 per cent., the liquid separates into two layers, but again becomes homogeneous as the proportion of nicotine reaches 82 per cent. When a solution containing 60 per cent. of nicotine and 40 per cent. of water is warmed, two layers form at 60°, but heating the mixture in a sealed tube restores homogeneity at 200°.

Other bases, such as β-picoline and methylpiperidine, exhibit similar behaviour towards water. In most instances a completely closed curve is not obtained. The system phenol—water gives only the upper part of the curve, for at low temperatures the component phenol separates in the solid state before homogeneity has been attained. For the system triethylamine—water it is possible to plot only the bottom part of the curve, the critical temperature of one of the components being reached before the liquid becomes homogeneous.

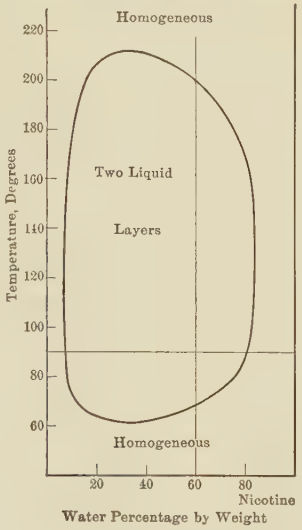


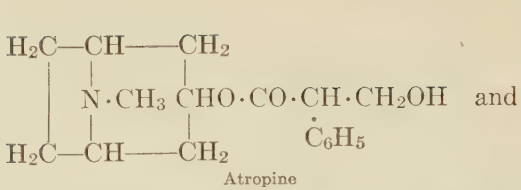
Fig. 79.—The System Nicotine—water.

Atropine, $C_{17}H_{23}O_3N$.

411. *Atropine* is present in the berry of the deadly nightshade (*Atropa belladonna*) and in the thorn-apple, the fruit of *Datura stramonium*. It is crystalline, melts at 115·5°, and is very poisonous. It exercises a "mydriatic" action, its dilute solution expanding the pupil of the eye, and for this reason it is employed in ophthalmic surgery. It is optically inactive. Heating it with hydrochloric acid or sodium hydroxide at 120° adds water and yields *tropine* and *tropic acid*:

$$\underset{\text{Atropine}}{C_{17}H_{23}O_3N} + H_2O = \underset{\text{Tropine}}{C_8H_{15}ON} + \underset{\text{Tropic acid}}{C_9H_{10}O_3}.$$

It can be regenerated from these two substances by the action of hydrogen chloride. Atropine is therefore the tropine ester of tropic acid (**324**). The constitutions of atropine and tropine are



This formula for tropine was proposed by WILLSTÄTTER, and is based on the decomposition-products of this substance. They are

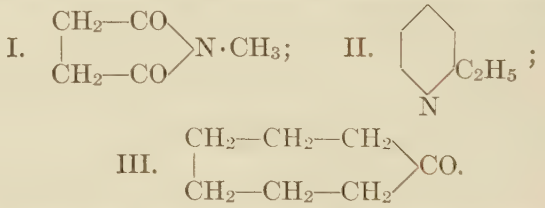
1. *Methylsuccinimide* (I), indicating the presence of a tetrahydropyrrole-nucleus (**395**).

2. *Tropidine*, obtained by elimination of water through heating with potassium hydroxide or dilute sulphuric acid:

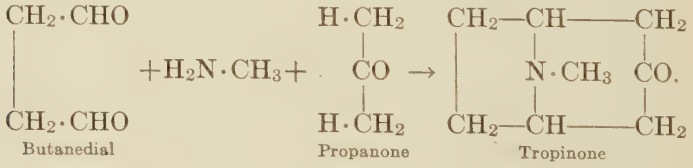
$$\underset{\text{Tropine}}{C_8H_{15}ON} - H_2O = \underset{\text{Tropidine}}{C_8H_{13}N}.$$

Tropidine can be converted into α-ethylpyridine (II), indicating tropine to contain a pyridine-ring.

Ecgonine (**412**) is a carboxylated tropine. It decomposes to suberone (III) demonstrating the presence of a ring of seven carbon atoms in the tropine molecule. Application of the usual methods has proved tropine to be a tertiary base, and to contain a hydroxyl-group:



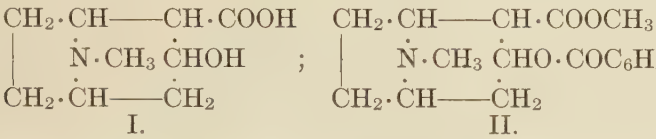
An important synthesis of *tropinone*, the ketone corresponding with tropine, has been effected by ROBINSON. It involves the condensation of butanedial, methylamine, and propanone:



Cocaine, $C_{17}H_{21}O_4N$.

412. On account of its value as a local anæsthetic, *cocaine* is the best-known of the alkaloids present in coca-leaves (*Erythroxylon coca*). It is crystalline, is readily soluble in alcohol, and melts at 98°. Heating

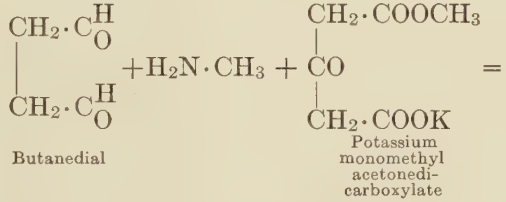
it with strong acids eliminates a benzoyl-group and a methyl-group, with formation of *ecgonine* (I), the constitution of cocaine being represented by II:



I. II.

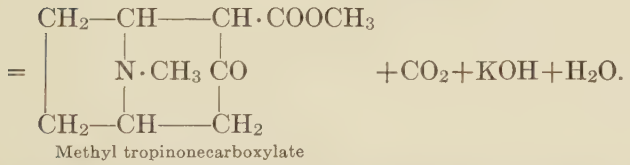
By benzoylating and methylating ecgonine, cocaine is regenerated. Ecgonine is a tropinecarboxylic acid.

The first step in WILLSTÄTTER's synthesis of cocaine is the interaction of butanedial, methylamine, and the potassium salt of monomethyl acetonedicarboxylate to give the methyl ester of *tropinonecarboxylic acid*:



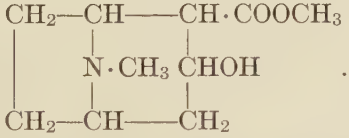
Butanedial

Potassium monomethyl acetonedicarboxylate



Methyl tropinonecarboxylate

Reduction of the ester of this ketonic acid with sodium-amalgam converts the CO-group into a CHOH-group, with formation of the methyl ester of ecgonine,



Benzoylation of this substance yields racemic cocaine. Both the optical isomerides of cocaine have also been prepared.

Morphine, $C_{17}H_{19}O_3N$.

413. *Morphine* is the longest-known alkaloid, having been obtained from opium by SERTÜRNER in 1806. Opium is the dried juice of the seed-capsules of *Papaver somniferum*, a variety of poppy. It is a very

complex mixture, containing caoutchouc; fats; resins; gums; carbohydrates; proteins; mineral salts; meconinic acid,

$$(CH_3O)_2C_6H_2(CH_2OH)(COOH);$$

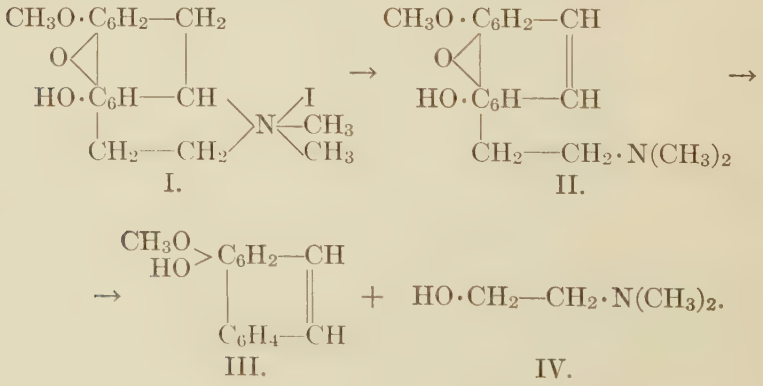
some more organic acids and other substances; and alkaloids. Twenty of these alkaloids have been identified, morphine being present in largest proportion, and constituting about ten per cent. of opium.

Morphine is crystalline, and melts with decomposition at 230°. It is slightly soluble in water, is without odour, and is employed as an anodyne and narcotic.

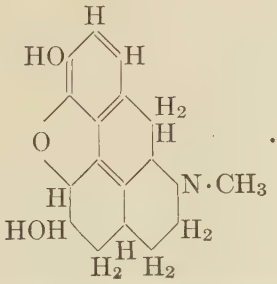
The reactions of morphine indicate one of its three oxygen atoms to form part of phenolic hydroxyl, proved by its solubility in alkalis; the second is present in alcoholic hydroxyl; and the third is united as in the ethers. Its distillation with zinc-dust yields phenanthrene, $C_{14}H_{10}$, these facts enabling the empirical formula to be expanded to

$$C_{17}H_{19}O_3N = C_3H_{16}N[C_{14}][O][OH][HOH].$$

The action of methyl iodide on its alkaline solution methylates the phenolic hydroxyl, and the simultaneous addition of methyl iodide at the nitrogen (I) proves morphine to be a tertiary base. The product formed is identical with the methyl-iodide derivative of codeine. Aqueous sodium hydroxide eliminates hydrogen iodide from this substance, and gives another tertiary base containing a like number of carbon atoms. It is termed *α-methylmorphimethine* (II). Heating methylmorphimethine with acetic anhydride yields a product free from nitrogen (III), and one containing nitrogen (IV). The first is *methylmorphol* or 4-*hydroxy*-3-*methoxy-phenanthrene*, convertible by further methylation into a synthetic product, dimethylmorphol (386), a reaction indicating its structure. The second is *dimethylhydroxyethylamine*, $CH_2OH \cdot CH_2 \cdot N(CH_3)_2$:



By combining these facts with others it has been possible to assign provisionally to morphine the structural formula

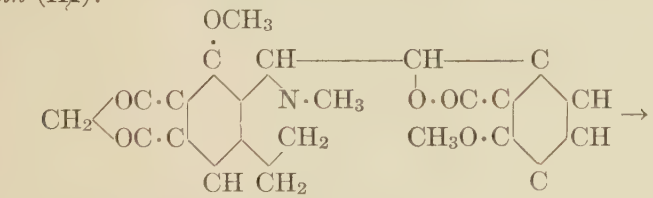


It represents morphine as a combination of a partially-hydrogenated dihydroxyphenanthrene containing an ether-linked oxygen atom and a hydrogenated pyridine-nucleus with its nitrogen atom in union with methyl.

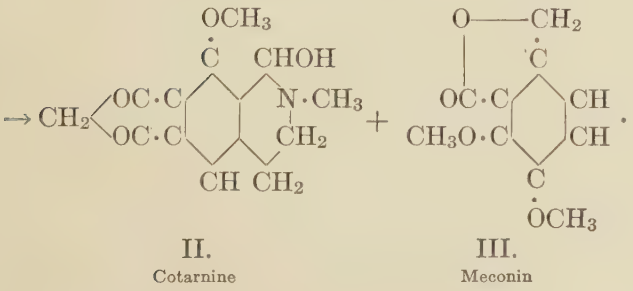
Heroine is the diacetyl-derivative of morphine; *codeine* is its monomethyl ether; and *thebaine* is the dimethyl ether of a tautomeric modification.

Narcotine, $C_{22}H_{23}O_7N$.

414. *Narcotine* is present in opium to the extent of about six per cent., its percentage being next to that of morphine. It is crystalline, melts at 176°, and is slightly poisonous. It is a weak tertiary base, its salts readily undergoing hydrolytic dissociation. It contains three methoxyl-groups, and has formula I. *Nornarcotine* has the formula $C_{19}H_{14}O_4N(OH)_3$. The hydrolysis of narcotine yields *cotarnine* (II), a derivative of *iso*quinoline, and the anhydride of meconinic acid, or *meconin* (III):



I. Narcotine



II. Cotarnine III. Meconin

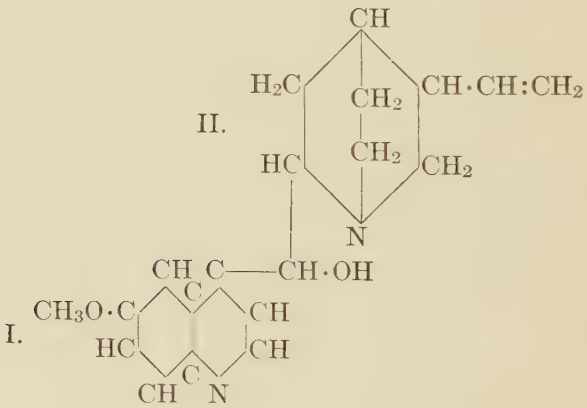
Quinine, $C_{20}H_{24}O_2N_2$.

415. The barks of certain trees of the *Cinchona* and *Remya* families contain a great number of alkaloids. The most important of them, on account of its anti-febrile effect, is *quinine*. *Cinchonine*, $C_{19}H_{22}ON_2$, is the next best-known. Its physiological action is similar to that of quinine, but is less pronounced.

In addition to alkaloids, these barks contain various acids such as quinic acid, quinovic acid, and quinotannic acid; and neutral substances such as quinovin and quina-red also are present.

Quinine is very slightly soluble in water, and is lævorotatory. In the anhydrous state it melts at 177°, but the trihydrate melts at 57°. It is a strong base, and both nitrogen atoms are tertiary. It unites with two equivalents of an acid. In dilute solution the salts of quinine exhibit a splendid blue fluorescence, a property serving as a test for the base.

The constitution of quinine has been elucidated, chiefly through the researches of Skraup and of Königs, the latter assigning to it the formula



according with the following properties of quinine. Its fusion with potassium hydroxide yields quinoline, p-*methylquinoline* or *lepidine* and p-*methoxyquinoline* from the part of the molecule numbered I in the structural formula; and β-ethylpyridine from part II. Its oxidation gives αβγ-pyridinetricarboxylic acid, also from part I. In addition, quinine is a ditertiary base, and contains a hydroxyl-group and a methoxyl-group. Its additive power indicates the presence of a double carbon bond.

Cinchonine has the simplest structure of any of the cinchona alkaloids, and differs from quinine in having methoxyl replaced by hydrogen. The other cinchona alkaloids are stereoisomerides of either cinchonine or quinine, exemplified by *cinchonidine* and *quinidine*; or they contain two additional hydrogen atoms, as in *hydroquinine* and its stereoisomerides, the vinyl-group CH_2:CH— having been changed into an ethyl-group. In *cupreine* a hydroxyl-group takes the place of the methoxyl-group of quinine.

The synthesis of the cinchona alkaloids from derivatives of quinoline and piperidine has been attained.

Strychnine, $C_{21}H_{22}O_2N_2$.

416. Three extremely poisonous alkaloids, *strychnine*, *brucine*, and *curarine*, are present in the seeds of *Strychnos nux vomica*, as well as in others of the *Strychnos* family. Little is known of the chemical nature of curarine, although it has been much studied from a physiological standpoint, its administration in small doses producing total paralysis. Strychnine and brucine cause death, preceded by tetanic spasms or muscular contraction; and curarine therefore is employed as an antidote.

Strychnine is crystalline, melts at 265°, and is almost insoluble in water. It is a monohydric tertiary base, only one of its nitrogen atoms exhibiting basic properties. Its fusion with potassium hydroxide yields quinoline and indole, and its distillation with slaked lime gives β-picoline (389). Heating with zinc-dust produces carbazole (382) and other substances.

In view of investigations made in conjunction with the late W. H. Perkin, jun., Robinson considers the chemical properties of strychnine to be represented most completely by the formula of Fig. 80.

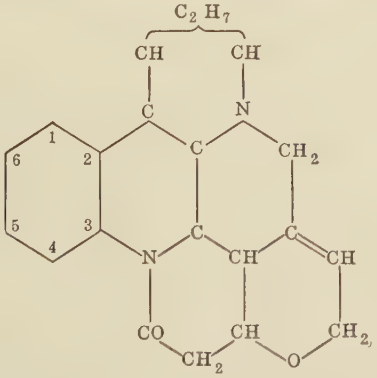


Fig. 80.—Robinson's Strychnine-formula.

The addition of the two carbon atoms and the seven hydrogen atoms shown in the formula must be assumed to involve the formation of two new rings, one of them being a bridged-ring.

Brucine differs from strychnine in having methoxyl-groups as substituents at positions 5 and 6.

INDEX

The basis of the arrangement of this index is threefold:
(1) The numbers refer to pages.
(2) In all instances of possible ambiguity as to the identity of the principal references, they are given in bold-face figures.
(3) Where a reference is a subdivision of a principal heading, it is indented one *em space* for each word of the principal heading not repeated. Portions of words followed by a hyphen are treated as words for the purposes of this arrangement.

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